ALTERNATING CURRENT POLAROGRAPHY OF ORGANIC COMPOUNDS

V. QUANTITATIVE TREATMENT OF THE ADSORPTION PROCESS

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Summary

Equations are derived to express the adsorption equilibrium subsisting at an adsorbent surface in the presence of two adsorbable species. These equations are applied to the case of the reduction of organic compounds at the dropping mercury electrode. It is well known that adsorption at the electrode can produce irreversibility in the D.C. step, and a qualitative explanation is provided. The same treatment is used to explain the shape of the A.C. calibration curves.

I. INTRODUCTION

In Part I of this series (Breyer, Bauer, and Hacobian 1954), salient features of the A.C. polarography of organic compounds were reported and discussed. It was stated that the calibration curves were typically non-linear, a fact qualitatively explicable in terms of adsorption processes.

In the present paper, equations are derived to express the adsorption-desorption equilibrium at the dropping mercury electrode for the case of simultaneous adsorption of the oxidized and reduced forms of a reversibly reduced depolarizer. By means of these equations a general expression is derived for the shape of the A.C. calibration curve.

The treatment also predicts that, in spite of a reversible reduction process, a D.C. polarographic step of the irreversible type will be obtained when the oxidized and reduced forms are adsorbed to a different extent.

II. THEORY AND DISCUSSION

The electrode-solution system is represented schematically in Figure 1. Spaces I and II together comprise the " potential-determining " region, that is, that space within which the electrode reaction occurs. Region I is the space occupied by adsorbed molecules. Region IV represents the bulk of the solution and region III is the " D.C. diffusion region " (cf. Breyer and Hacobian 1954).

This representation is purely pictorial ; for instance, regions I and II may, in actual fact, be spatially coincident. It is more convenient, however, to consider adsorbed and unadsorbed molecules in separate regions, rather than as energetically different molecules occupying the same region.

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(*a*) *Quantitative Treatment of the Adsorption Equilibrium*

Let $C_{Ox\,I}$, $C_{R\,I}$ be the concentrations of oxidized and reduced forms respectively in region I; $C_{Ox\,II}$, $C_{R\,II}$ the respective concentrations in region II; and θ_{Ox} $(=sC_{Ox\,I})$, θ_R $(=sC_{R\,I})$ the fractions of the surface of the electrode covered by adsorbed oxidized and reduced molecules respectively, assuming implicitly that oxidized and reduced molecules are of the same size in the adsorbed state.

Considering a steady state of the electrode-solution system, at the time instant of the maximum size of the mercury drop, the following equations can

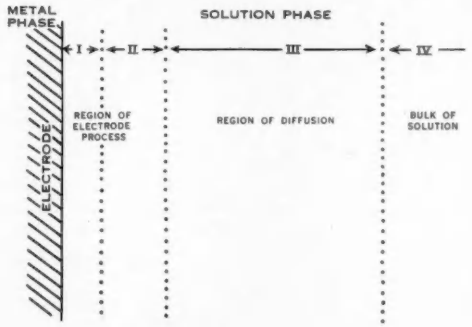

Fig. 1

be written, by analogy with Langmuir's treatment of physical adsorption (Langmuir 1918):

rate of adsorption of oxidized form $= kC_{Ox\,II}\alpha_1(1-\theta_{Ox}-\theta_R)+kC_{Ox\,II}\alpha_2\theta_R$,

rate of desorption of oxidized form $= \nu_{Ox}\theta_{Ox}+kC_{R\,II}\beta_2\theta_{Ox}$,

rate of adsorption of reduced form $= kC_{R\,II}\beta_1(1-\theta_{Ox}-\theta_R)+kC_{R\,II}\beta_2\theta_{Ox}$,

rate of desorption of reduced form $= \nu_R\theta_R+kC_{Ox\,II}\alpha_2\theta_R$,

where $kC_{Ox\,II}$, $kC_{R\,II}$ are the numbers of molecules (of oxidized and reduced forms respectively) arriving at the electrode surface per unit time;

α_1, α_2 the fractions of these adhering on free surface;

β_1, β_2 the fractions which displace molecules of the other form from the surface;

ν_{Ox}, ν_R the fractions of the number of molecules in the adsorbed state which are spontaneously desorbed per unit time.

At equilibrium

$$kC_{Ox\,II}\alpha_1(1-\theta_{Ox}-\theta_R)+kC_{Ox\,II}\alpha_2\theta_R=\nu_{Ox}\theta_{Ox}+kC_{R\,II}\beta_2\theta_{Ox}, \quad \ldots\ (1)$$

and

$$kC_{R\,II}\beta_1(1-\theta_{Ox}-\theta_R)+kC_{R\,II}\beta_2\theta_{Ox}=\nu_R\theta_R+kC_{Ox\,II}\alpha_2\theta_R. \quad \ldots\ (2)$$

At the summit potential, $\theta_{Ox}=\theta_R=\theta$ say (Breyer, Bauer, and Hacobian 1954); solving equations (**1**) and (**2**) for this condition,

$$\theta=\frac{b_{Ox}C_{Ox\,II}}{1+b''_RC_{R\,II}+2b_{Ox}C_{Ox\,II}-b'_{Ox}C_{Ox\,II}}=\frac{b_RC_{R\,II}}{1+b''_{Ox}C_{Ox\,II}+2b_RC_{R\,II}-b'_RC_{R\,II}}, \quad \ldots\ldots\ldots (3)$$

where

$$\left.\begin{aligned} b_{Ox}&=k\frac{\alpha_1}{\nu_{Ox}}, \quad b'_{Ox}=k\frac{\alpha_2}{\nu_{Ox}}, \quad b''_{Ox}=k\frac{\alpha_2}{\nu_R}=b'_{Ox}\frac{\nu_{Ox}}{\nu_R},\\ b_R&=k\frac{\beta_1}{\nu_R}, \quad b'_R=k\frac{\beta_2}{\nu_R}, \quad b''_R=k\frac{\beta_2}{\nu_{Ox}}=b'_R\frac{\nu_R}{\nu_{Ox}}. \end{aligned}\right\} \quad \ldots\ldots\ldots (4)$$

Here, b_{Ox} is the Langmuir adsorption coefficient of the oxidized form at the free electrode surface, whereas b'_{Ox} is the adsorption coefficient of the oxidized form displacing reduced molecules and b_R, b'_R are the corresponding adsorption coefficients of the reduced molecules.

Under normal polarographic conditions, the total concentration of depolarizer (sum of the concentrations of the oxidized and reduced forms) in region II is the same as in the bulk of the solution. Thus,

$$C_{Ox\,II}+C_{R\,II}=C, \quad \ldots\ldots\ldots\ldots\ldots (5)$$

where C represents the concentration of depolarizer in the bulk.

Putting

$$C_{Ox\,II}=xC, \quad \ldots\ldots\ldots\ldots\ldots (6)$$

we have

$$C_{R\,II}=(1-x)C,$$

where x may or may not be a function of C. Substituting (**6**) in equation (**3**),

$$\theta=\frac{b_{Ox}xC}{1+b''_RC+(2b_{Ox}-b'_{Ox}-b''_R)xC}=\frac{b_R(1-x)C}{1+(2b_R-b'_R)C+(b''_{Ox}+b'_R-2b_R)xC}. \quad \ldots\ldots\ldots\ldots (7)$$

Expanding this equation,

$$xb_{Ox}+xb_{Ox}(2b_R-b'_R)C+x^2b_{Ox}(b''_{Ox}+b'_R-2b_R)C=(1-x)b_R+(1-x)b_Rb''_RC+x(1-x)b_R(2b_{Ox}-b'_{Ox}-b''_R)C. \quad \ldots\ldots\ldots\ldots (8)$$

Equation (**8**) cannot be simplified without making some assumptions about the relative values of the adsorption coefficients. It can be seen that x is a function of both C and of the adsorption coefficients. The fact that x depends on C shows that, with varying bulk concentration, there is a change in both the absolute and relative concentrations of oxidized and reduced forms in region II at the summit potential.

In the following, equation (**8**) is solved for the special case, where x is independent of C. By equating coefficients of C we obtain

$$x=\frac{b_R}{b_R+b_{Ox}}, \quad \ldots\ldots\ldots\ldots\ldots (9)$$

and also

$$xb_{Ox}(2b_R - b'_R) + x^2 b_{Ox}(b''_{Ox} + b'_R - 2b_R) = (1-x)b_R b''_R + x(1-x)b_R(2b_{Ox} - b'_{Ox} - b''_R). \quad \ldots\ldots\ldots\ldots (10)$$

Substituting for x in equation (**10**) and simplifying,

$$b_R(b''_{Ox} + b'_{Ox}) = b_{Ox}(b''_R + b'_R), \quad \ldots\ldots\ldots\ldots (11)$$

and using equation (**4**),

$$b_R \alpha_2 = b_{Ox} \beta_2. \quad \ldots\ldots\ldots\ldots (12)$$

Since b_{Ox}, b_R represent the adsorption coefficients of the two forms on the free surface, while α_2, β_2 represent " displacement coefficients " of one form by the other, equation (**12**) will be obeyed when the two forms have the same adsorptive properties.

In this case, $b_R = b_{Ox} = b$, say, and $b''_{Ox} = b'_{Ox}$ (eqn. (**4**)), so that equation (**7**) reduces to

$$\theta = \frac{1}{2} \cdot \frac{bC}{1+bC}. \quad \ldots\ldots\ldots\ldots (13)$$

(b) Shape of the D.C. Step

Where the electroactive species are not adsorbed, their relative concentrations are the same in regions I and II and are determined only by the electrode potential. However, when adsorption occurs, the adsorbed molecules in region I, that is, in the rigid double layer, will be far more affected by the potential of the electrode than will unadsorbed molecules in region II. In this case the relative concentrations of the electroactive species in region I will be potential-determined, while the concentrations in region II will be determined by the adsorption equilibrium.

In the case where the adsorbed molecules undergo a reversible change we have

$$E = E_0 + \frac{RT}{nF} \ln \left(\frac{C_{Ox\,I}}{C_{R\,I}} \right). \quad \ldots\ldots\ldots\ldots (14)$$

Solving equations (**1**) and (**2**) without the assumption that $\theta_{Ox} = \theta_R$, we obtain

$$\theta_{Ox} = \frac{kC_{Ox\,II}\alpha_1(1-\theta_R) + kC_{Ox\,II}\alpha_2\theta_R}{\nu_{Ox} + kC_{R\,II}\beta_2 + kC_{Ox\,II}\alpha_1}, \quad \ldots\ldots\ldots (15)$$

and

$$\theta_R = \frac{kC_{R\,II}\beta_1(1-\theta_{Ox}) + kC_{R\,II}\beta_2\theta_{Ox}}{\nu_R + kC_{Ox\,II}\alpha_2 + kC_{R\,II}\beta_1}. \quad \ldots\ldots\ldots (16)$$

Combining (**15**) and (**16**) and rearranging,

$$\frac{\theta_{Ox}}{\theta_R} = \frac{C_{Ox\,I}}{C_{R\,I}} = \frac{C_{Ox\,II}}{C_{R\,II}} \cdot \frac{\alpha_1\nu_R + k\alpha_1\alpha_2 C_{Ox\,II} + k\beta_1\alpha_2 C_{R\,II}}{\beta_1\nu_{Ox} + k\beta_1\beta_2 C_{R\,II} + k\alpha_1\beta_2 C_{Ox\,II}}. \quad \ldots (17)$$

Thus, in the general case $C_{\mathrm{Ox\,I}}/C_{\mathrm{R\,I}} \neq C_{\mathrm{Ox\,II}}/C_{\mathrm{R\,II}}$, that is, whilst the changes of concentration with potential in region I follow the reversible electrode equation, the concentration changes in region II do not follow it. Now the shape of the D.C. step depends on the ratio of concentrations of oxidized and reduced forms in region II, and since in the contemplated case this ratio does not satisfy equation (**14**), the D.C. step will not obey the Heyrovský-Ilkovič equation

$$E = E_{\frac{1}{2}} + \frac{RT}{nF} \ln \left(\frac{i_\alpha - i}{i} \right). \qquad \ldots\ldots\ldots\ldots \quad (18)$$

In other words, the D.C. step is of the irreversible type.

In the special case where oxidized and reduced forms are equally adsorbable, that is, when $\alpha_1 = \beta_1$, $\alpha_2 = \beta_2$, and $\nu_{\mathrm{Ox}} = \nu_{\mathrm{R}}$, equation (**17**) reduces to $C_{\mathrm{Ox\,I}}/C_{\mathrm{R\,I}} = C_{\mathrm{Ox\,II}}/C_{\mathrm{R\,II}}$ and the D.C. step will be of the reversible type.

Van Rysselberghe (1946, 1951) has used the Freundlich isotherm to show that adsorption and/or polymerization will make the polarographic step deviate in shape from the reversible type, a conclusion also reached by the treatment adopted in the present paper.

(*c*) *Height of the A.C. Wave*

The height of the A.C. wave of an organic compound is given by (Breyer, Bauer, and Hacobian 1954)

$$i_{\sim(E_s)} = y\beta_{(E_s)} C_{\mathrm{I}\,(E_s)}, \qquad \ldots\ldots\ldots\ldots\ldots \quad (19)$$

where $i_{\sim(E_s)}$ is the height of the wave, $C_{\mathrm{I}\,(E_s)}$ $(=\theta/s)$ is the concentration of either oxidized or reduced form in region I at the summit potential, and y and $\beta_{(E_s)}$ are proportionality factors which depend on the number of electrons involved, on the type of the electrode reaction, and on the frequency and amplitude of the alternating voltage.

Using equation (**7**), we have

$$i_{\sim(E_s)} = \frac{y' b_{\mathrm{Ox}} x C}{1 + b'_{\mathrm{R}} C + (2b_{\mathrm{Ox}} - b'_{\mathrm{Ox}} - b'_{\mathrm{R}}) x C}, \qquad \ldots\ldots\ldots \quad (20)$$

where $y' = y\beta_{(E_s)}/s$. In the special case where oxidized and reduced forms are equally adsorbed, we obtain from equation (**13**)

$$i_{\sim(E_s)} = \frac{1}{2} \cdot \frac{y' b C}{1 + b C}. \qquad \ldots\ldots\ldots\ldots \quad (21)$$

The coefficients of C in equation (**21**) denote adsorption coefficients; however, in the general expression (**20**) these coefficients include the variable x and hence are not simply adsorption coefficients.

The experimentally observed calibration curves are of the general form

$$i_{\sim(E_s)} = \frac{abC}{1 + bC} \left(1 + \frac{\alpha\beta C}{1 + \beta C} \right), \qquad \ldots\ldots\ldots \quad (22)$$

where α may be positive, or negative, or zero. In the case of quinone (Breyer and Bauer 1955*a*), or in the case of the second wave of chloranilic acid at pH 2·2

(Breyer and Bauer 1955*b*), as well as with *peri*naphthenone (Breyer and Bauer 1955*c*), $\alpha=0$ and the calibration curves follow the relation

$$i_{\sim(E_g)}=\frac{abC}{1+bC}. \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (23)$$

For quinone, $b=4\cdot2\times10^3$ l. mole^{-1} at 20 °C and $1\cdot45\times10^4$ l. mole^{-1} at 3 °C; for the second wave of chloranilic acid at pH 2·2, $b=4\cdot6\times10^3$ l. mole^{-1} at 20 °C and $2\cdot1\times10^4$ l. mole^{-1} at 3 °C. This increase with decreasing temperature is typical of an adsorption coefficient, so that we may correlate equation (**23**) with the theoretically derived relationship (**21**).

Calibration curves following equation (**22**) can be regarded as corresponding to the general theoretical expression (**20**), since both these equations represent curves which deviate to a greater or lesser extent from the simple expressions (**23**) and (**21**). Also for calibration curves following equation (**22**), the parameters b and β have not always been found to increase with decreasing temperature (see Table 1), and consequently do not represent simple adsorption coefficients, a fact which seems to justify correlating the empirical equation (**22**) with equation (**20**).

TABLE 1

EFFECT OF TEMPERATURE ON THE PARAMETERS DESCRIBING THE A.C. CALIBRATION CURVES OF CHLORANILIC ACID

pH	20 °C		3 °C	
	b ($\times10^4$ l. mole^{-1})	β ($\times10^4$ l. mole^{-1})	b ($\times10^4$ l. mole^{-1})	β ($\times10^4$ l. mole^{-1})
2·2*	7·4	3·1	6·5	3·0
4·9	6·1	4·5	7·4	3·3
7·1	3·7	4·2	7·8	—

* First wave.

It is known that the adsorptive properties vary with the potential at the adsorbent surface. Consideration of this factor has been omitted in the present treatment for the sake of simplicity, but it might be mentioned that if the summit potential changes with concentration, the adsorption coefficient of equations (**20**) and (**21**), as well as the variable x, will also change. This demonstrates another reason why calibration curves might deviate from the equation (**23**).

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THE INFLUENCE OF THE SUPPORTING ELECTROLYTE ON TENSAMMETRIC WAVES

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Summary

The influence of the supporting electrolyte on the height and frequency dependence of tensammetric waves is examined. Anions generally affect the positive tensammetric waves whereas cations have little effect on either positive or negative waves. A tentative explanation of the underlying phenomena is given and the possible mechanism discussed.

I. Introduction

It is known that when a small sinusoidal alternating voltage is superimposed onto the direct potential applied to a dropping mercury electrode in the presence of surface active molecules, wave shaped current-voltage curves (tensammetric waves) are obtained (Breyer and Hacobian 1952; Doss and Kalyanasundaram 1952*a*, 1952*b*). This current-voltage curve consists essentially of two waves situated on either side of the electrocapillary zero point. The waves were called positive and negative tensammetric waves respectively and are shown in Figure 1. At high positive or negative polarization the tensammetric curve coincides with that of the supporting electrolyte, that is, desorption takes place. In the region between the two waves the tensammetric curve is depressed compared with the curve of the supporting electrolyte. This is due to the fact that the double layer capacity is considerably lowered by the presence of the adsorbed layer at the electrode/solution interface.

Examination of the tensammetric potentials and wave heights of a number of surface active substances showed that the supporting electrolyte has a marked influence on the height and frequency dependence of tensammetric waves. It was felt that little information regarding tensammetric behaviour could be obtained until this influence was comprehensively studied.

II. Charge Density and Tensammetric Current

The adsorption/desorption equilibrium at the electrode surface can be visualized as the outcome of a competition between (i) the forces responsible for adsorption of the surface active molecules onto the electrode and (ii) the attraction forces between the electrode and the ions of the supporting electrolyte, tending to displace the surface active molecules from the interface. Quite generally the tensammetric current is due to the oscillatory movement of both the dipoles and the ions of the supporting electrolyte (cf. Breyer and Hacobian

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1952). The current contribution of dipoles and ions depends (*a*) on their polarizability and (*b*) on the number of permanent (ionic) charges they might possess.

The current contribution of the supporting electrolyte ions is measured by the base current i_b, which in turn depends upon the value of the charge density at the mercury surface. It seems noteworthy that whereas the base current, corresponding to the positive tensammetric potential i_{b+}, changed appreciably, the base current, corresponding to the negative tensammetric potential i_{b-}, remained fairly constant when the supporting electrolyte was

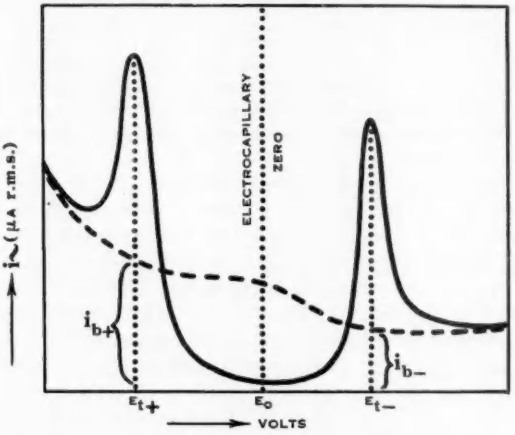

Fig. 1.—Schematic representation of tensammetric waves.
—— Tensammetric curve.
---- A.C. polarogram of supporting electrolyte alone.
E_{t+}, E_{t-}, Summit potentials of positive and negative tensammetric waves respectively.
i_{b+}, Base current corresponding to E_{t+}.
i_{b-}, Base current corresponding to E_{t-}.

changed. This is in accordance with the fact that adsorbed anions are able to move closer to the electrode/solution interface than cations (Grahame 1951, 1952). The i_{b+} value was highest in the presence of $SO_4^{=}$ ions, less in the case of NO_3^- ions and least in solutions containing ClO_4^- ions. One can thus conclude that the charge density at the mercury surface is greatest when the electrode is populated by $SO_4^{=}$ ions, a result which is in keeping with that obtained by Grahame from capacitance measurements (Grahame loc. cit.). In the region corresponding to negative polarization the cations of the supporting electrolyte play a dominant role. It is well known that generally the Helmholtz-Gouy capacitance of the electrical double layer varies but little with the nature of the cations in solution. This has been explained on the grounds that, unlike anions, cations show little or no specific adsorption and are generally separated from the electrode surface by a solvent sheath (Grahame 1947). It is therefore to be

expected that the negative charge density at the electrode will vary but litte with the nature of the supporting electrolyte.

It should be expected that for one and the same surface active compound, a direct correlation exists between the tensammetric current ($i_{(E_t)}$) and the base current (i_b) in different supporting electrolytes. To test this assumption the influence of the supporting electrolyte on the tensammetric current of different alcohols was studied. The results obtained with ethanol, *n*-amyl alcohol, and *cyclo*hexanol are shown in Tables 1, 2, and 3.

TABLE 1

TENSAMMETRIC BEHAVIOUR OF 5M ETHANOL IN VARIOUS SUPPORTING ELECTROLYTES

A.C. 15 mV r.m.s. ; *T*, 25 °C air-free solutions

Supporting Electrolyte (N solution)	i_{b+}	i_{b-}	$i_{(E_{t+})}$	$i_{(E_{t-})}$	E_{t+} (V *v.* S.C.E.)	E_{t-} (V *v.* S.C.E.)
	(μA r.m.s.)					
$HClO_4$	2·0	—*	1·1	—*	−0·240	—*
NH_4ClO_4	2·2	2·3	1·1	0·9	−0·186	−1·300
$NaClO_4$	2·1	2·0	0·9	1·0	−0·176	−1·340
H_2SO_4	4·2	—*	3·6	—*	−0·080	—*
$(NH_4)_2SO_4$ ..	4·4	2·2	5·0	1·1	−0·131	−1·351
Na_2SO_4	4·6	2·0	4·7	1·1	+0·001	−1·380
$MgSO_4$	4·6	2·2	6·4	0·9	−0·041	−1·380
$NaHSO_4$ ..	4·0	—*	4·5	—*	−0·056	—*
HNO_3	2·3	—*	2·2	—*	−0·220	—*
NH_4NO_3	2·5	2·0	2·0	1·1	−0·226	−1·301
$NaNO_3$	2·4	2·2	2·4	1·1	−0·170	−1·341
KNO_3	2·5	2·0	2·1	1·0	−0·221	−1·300
HCl	4·0	—*	3·6	—*	−0·240	—*
NH_4Cl	4·2	2·0	3·2	0·9	−0·222	−1·360
NaCl	4·2	2·0	4·0	1·1	−0·209	−1·360
KCl	4·3	2·0	4·1	1·1	−0·210	−1·327
$MgCl_2$	4·3	2·0	3·7	0·9	−0·213	−1·290

* Hydrogen discharge interferes.

Similar results were obtained with methyl, *n*-propyl, *n*-butyl, and *n*-octyl alcohols. In the tables the symbols $i_{(E_{t+})}$ and $i_{(E_{t-})}$ stand for the tensammetric current values of the corresponding positive and negative tensammetric waves at the peak potentials E_{t+} and E_{t-}. The $i_{(E_{t+})}$ values changed appreciably with the nature of the supporting electrolyte, in contradistinction to $i_{(E_{t-})}$ values which remained fairly constant (cf. Tables 1, 2, and 3). This can be explained from the reasoning that the higher charge density found at positive polarizations, must in turn lead to larger variations in permittivity with applied potential ($\delta k/\delta E$), a quantity on which the value of the current of all A.C. processes depends (Breyer 1953). Accordingly it is also found that $i_{(E_{t-})}$ changes but

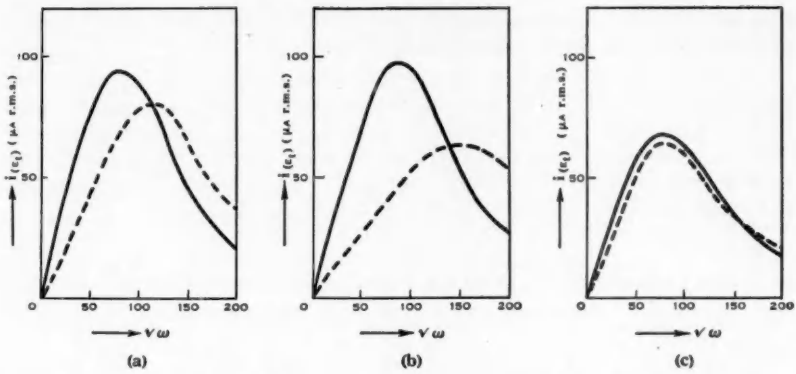

Fig. 2.—$i_{(E_t)}/\sqrt{\omega}$ curves of the tensammetric waves of some alcohols in M Na_2SO_4.
A.C. 15 mV r.m.s.; T, 20 °C; air-free solutions.

—— Positive waves.
---- Negative waves.
(*a*) 0·1M *cyclo*hexanol.
(*b*) Saturated octyl alcohol.
(*c*) M *n*-propyl alcohol.

TABLE 2

TENSAMMETRIC BEHAVIOUR OF 0·1M *n*-AMYL ALCOHOL IN VARIOUS SUPPORTING ELECTROLYTES
A.C. 15 mV r.m.s.; T, 25 °C

Supporting Electrolyte (N solution)	i_{b+}	i_{b-}	$i_{(E_t+)}$	$i_{(E_t-)}$	E_{t+} (V *v.* S.C.E.)	E_{t-} (V *v.* S.C.E.)
	(μA r.m.s.)					
$HClO_4$	2·0	2·3	4·6	4·0	−0·159	−1·220
NH_4ClO_4	2·3	2·1	5·6	4·9	−0·081	−1·090
$NaClO_4$	2·1	2·0	5·2	4·3	−0·098	−1·118
H_2SO_4	4·7	2·4	22·5	4·1	−0·093	−1·131
$(NH_4)_2SO_4$ ..	4·9	2·0	32·0	5·0	−0·002	−1·201
Na_2SO_4	4·9	2·1	39·2	6·9	+0·032	−1·262
K_2SO_4	4·8	2·2	29·0	5·0	+0·001	−1·198
$MgSO_4$	4·8	2·1	30·5	4·6	+0·056	−1·248
$NaHSO_4$ ..	4·6	1·9	33·9	6·5	−0·032	−1·260
HNO_3	2·4	—*	10·1	—*	−0·207	—*
NH_4NO_3	2·6	2·1	11·8	4·9	−0·161	−1·059
$NaNO_3$	2·7	1·9	11·3	6·5	−0·118	−1·152
KNO_3	2·6	2·1	10·1	4·6	−0·143	−1·143
HCl	4·6	1·9	16·9	4·8	−0·229	−1·200
NH_4Cl	4·4	2·0	19·5	4·9	−0·188	−1·111
NaCl	4·4	2·0	25·7	5·6	−0·166	−1·122
KCl	4·5	2·0	26·0	5·5	−0·180	−1·119
$MgCl_2$	4·5	2·2	26·9	5·2	−0·191	−1·099

* Hydrogen discharge interferes.

little with the nature of the supporting electrolyte since the charge densities at negative polarizations are more or less the same in all electrolytes examined.

III. Field Frequency and Tensammetric Current

Figure 2 shows that the $i_{(E_t)}/\sqrt{\omega}$ plots of some alcohols in M Na_2SO_4 as supporting electrolyte.

The frequency at which a maximum current is obtained, $\omega_{max.}$, is a measure of the rate of the electrode process (Breyer, Bauer, and Hacobian 1955). It

Table 3

TENSAMMETRIC BEHAVIOUR OF 0·05M *cyclo*HEXANOL IN VARIOUS SUPPORTING ELECTROLYTES

A.C. 15 mV r.m.s.; T, 25 °C

Supporting Electrolyte (0·5N solution)	i_{b+}	i_{b-}	$i_{(E_{t+})}$	$i_{(E_{t-})}$	E_{t+} (V *v.* S.C.E.)	E_{t-} (V *v.* S.C.E.)
	(μA r.m.s.)					
$HClO_4$	2·0	1·9	4·1	4·9	−0·100	−1·308
NH_4ClO_4	2·2	2·2	4·8	6·5	−0·060	−1·178
$NaClO_4$	2·1	1·9	5·2	5·2	−0·034	−1·186
H_2SO_4	4·4	1·9	19·4	4·2	−0·019	−1·193
$(NH_4)_2SO_4$ ..	4·9	2·2	32·0	7·7	−0·0145	−1·209
Na_2SO_4	4·9	2·0	30·3	9·2	−0·002	−1·234
K_2SO_4	4·8	2·2	33·0	9·2	−0·002	−1·216
$MgSO_4$	5·0	2·0	28·8	7·5	−0·007	−1·160
$NaHSO_4$ ..	4·3	1·9	23·2	5·0	−0·027	−1·235
HNO_3	2·6	—*	10·2	—*	−0·135	—*
NH_4NO_3	2·8	2·0	9·0	5·2	−0·120	−1·130
$NaNO_3$	2·9	2·0	7·1	4·9	−0·100	−1·171
KNO_3	2·9	1·9	7·6	5·0	−0·101	−1·171
HCl	—	1·9	—	4·2	—	−1·220
NH_4Cl	—	2·0	—	7·2	—	−1·173
NaCl	—	2·0	—	7·1	—	−1·210
KCl	—	2·0	—	6·2	—	−1·211
$MgCl_2$	—	2·1	—	5·0	—	−1·189

* Hydrogen discharge interferes.

can be seen that the rates of the process occurring at E_{t-} are greater than the corresponding ones at E_{t+}.

An increased force of attraction between ion and electrode leads to an increased surface charge density. Now, it seems reasonable to assume that an increased force of attraction results in an increased hindrance of the adsorption/desorption process at the electrode, with the consequent lowering of the tensammetric rate constant. Since it is a measure of the charge density, it follows that the tensammetric process should follow field changes to higher frequencies in those electrolytes whose ions give rise to low i_b values.

This conclusion has been tested experimentally. Thus for instance with Na_2SO_4 as supporting electrolyte, $SO_4^{=}$ ions are, as already mentioned, more strongly bonded to the electrode surface than Na^+ ions and hence the i_{b+} values result substantially higher than the i_{b-} values. In accordance with the above

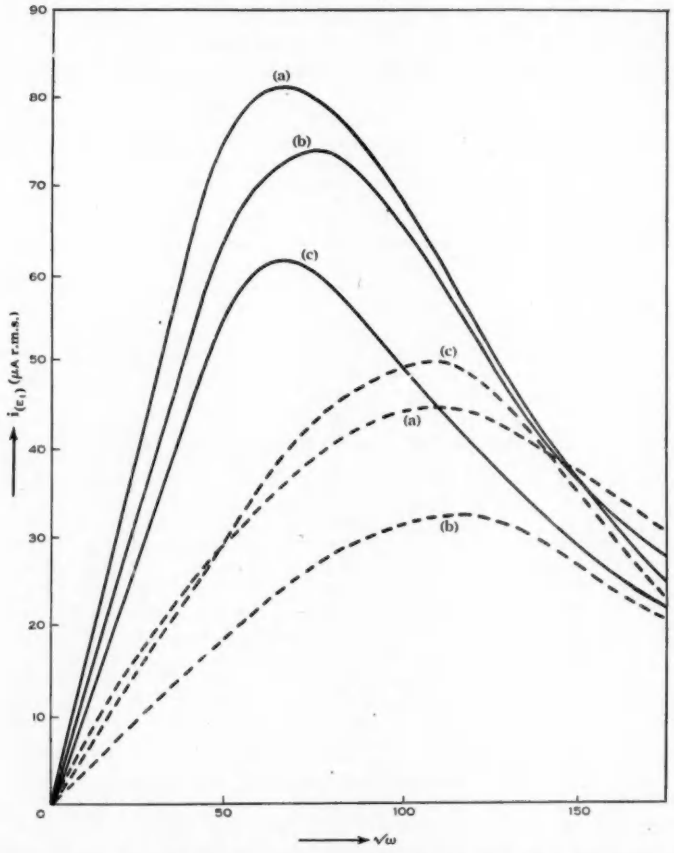

Fig. 3.—$i_{(Et)}/\sqrt{\omega}$ curves of 0·5M *n*-amyl alcohol in (*a*) N Na_2SO_4, (*b*) N $NaNO_3$, (*c*) 0·5N $NaClO_4$, as supporting electrolytes. A.C. 15 mV r.m.s.; *T*, 20 °C; air-free solutions.
—— Positive waves.
---- Negative waves.

reasoning it was found (Figs. 2 and 3) that the tensammetric process occurring at E_{t-} follows the field to higher frequencies than does the process at E_{t+}. The same type of behaviour was encountered with other supporting electrolytes (cf. Figs. 3(*a*) and 3(*b*)).

Tensammetric processes in $NaClO_4$ are of particular interest. It was found that both the wave heights and frequency dependence at E_{t+} and E_{t-} differ least in $NaClO_4$ as supporting electrolyte (Fig. 3(*c*)). It seems, therefore, that in this case the force of attraction exerted by the electrode on either anion or cation is approximately equal.

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POLAROGRAPHY OF SOME COORDINATION COMPOUNDS OF PLATINUM

III. IONS OF THE TETRAMMINEPLATINUM(II) TYPE

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Summary

A number of tetrammine ions of divalent platinum, in which the ligands were ammonia, methylamine, dimethylamine, ethylenediamine, pyridine, aniline, and combinations of some of these, were studied at the dropping mercury electrode. Some of the ions showed maxima in their current-voltage curves (c-v curves). The formation of hydrogen interfered with the c-v curves of other ions, so that limiting currents were not obtainable. A method was devised for the measurement of a voltage by means of which the ease of reduction of the ions could be compared. Using a supporting electrolyte of 0·1M KCl and 0·01% gelatin, the order of increasing ease of reduction was found to be

$$[Pt\{(CH_3)_2NH\}_4]^{2+} = [Pt(NH_3)_4]^{2+} = [Pt(NH_3)_3(C_5H_5N)]^{2+} = [Pt\{C_2H_4(NH_2)_2\}_2]^{2+}$$
$$< cis\text{-}[Pt(NH_3)_2(C_5H_5N)_2]^{2+} < trans\text{-}[Pt(NH_3)_2(C_5H_5N)_2]^{2+}$$
$$< [Pt(CH_3NH_2)_4]^{2+} = [Pt(NH_3)(C_5H_5N)_3]^{2+} < [Pt(C_5H_5N)_4]^{2+}$$
$$< cis\text{-}[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+} < trans\text{-}[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}.$$

When the ammonia groups of $[Pt(NH_3)_4]^{2+}$ were successively replaced by pyridine groups, the resulting c-v curves shifted progressively to more positive voltages. It was also found that *cis*- and *trans*-isomers of $[PtA_2B_2]^{2+}$ reduced at different voltages. The *trans*-isomer reduced more readily.

I. INTRODUCTION

The platinum(II) complexes were studied to ascertain the possible existence of monovalent platinum compounds. At the same time, the effect of changing the coordinated groups upon the reduction behaviour of the ions was investigated. The behaviour of some ammines of platinum(IV) at the dropping mercury electrode (D.M.E.) was described in preceding papers (Hall and Plowman 1955*a*, 1955*b*).

II. EXPERIMENTAL

(*a*) *Apparatus and Materials*

The apparatus previously described (Hall and Plowman 1955*a*, p. 159) was employed. The capillary had the following characteristics: $m = 1 \cdot 50$ mg sec^{-1}; drop time $= 4 \cdot 8$ sec under a pressure of $50 \cdot 0$ cm Hg.

The material A.R. KCl was used.

(*b*) *Preparation of Compounds*

(i) *Tetrammineplatinum(II) Perchlorate and* (ii) *Bis(ethylenediamine)-platinum(II) Chloride.* The preparation of these compounds was described in Part I of this series (Hall and Plowman 1955*a*, p. 160).

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(iii) *Tetrakis(methylamine)platinum(II) Chloride.* This compound was first prepared by Jorgensen (1886). The following procedure was carried out: a solution of potassium tetrachloroplatinate(II) and methylamine hydrochloride was heated with the gradual addition of methylamine solution in excess until pale yellow in colour. The solution was acidified and evaporated at 100 °C. The crystalline material which separated out was filtered off and dissolved in warm aqueous methylamine. Evaporation yielded a white crystalline compound which was recrystallized twice from water-acetone (Found : Pt, 50·0 ; N, 14·3%. Calc. for $[Pt(CH_3NH_2)_4]Cl_2$: Pt, 50·0 ; N, 14·4%).

(iv) *Tetrakis(dimethylamine)platinum(II) Perchlorate.* Jorgensen (1906) prepared a solution of the chloride of this cation but did not isolate the product. The following procedure was used: a mixture of potassium tetrachloroplatinate(II), dimethylamine hydrochloride, and dimethylamine was allowed to stand at room temperature for several days. Golden yellow crystals of dichlorobis(dimethylamine)platinum(II) precipitated and were recrystallized from boiling water (Found : Pt, 54·2%. Calc. for $[Pt\{(CH_3)_2NH\}_2Cl_2]$: Pt, 54·8%). This compound when stirred for 24 hr at room temperature with concentrated aqueous dimethylamine gradually dissolved to give a clear greenish yellow solution, which was poured into a concentrated solution of sodium perchlorate. The white crystalline precipitate was recrystallized three times from hot water. The salt was soluble in acetone, insoluble in ether, and sparingly soluble in cold water (Found : Pt, 33·8 ; N, 9·9%. Calc. for $[Pt\{(CH_3)_2NH\}_4](ClO_4)_2$: Pt, 34·0 ; N, 9·8%).

(v) *Tetrapyridineplatinum(II) Perchlorate.* The procedure of Drew *et al.* (1932) was mainly followed for the preparation of the chloride of this cation and of those where pyridine was successively replaced by ammonia. Aqueous pyridine, added to a solution of potassium tetrachloroplatinate(II) at room temperature, gradually precipitated pale yellow dichlorodipyridineplatinum(II). This compound was separated and warmed with aqueous pyridine to produce a clear colourless solution from which tetrapyridineplatinum(II) chloride 3-hydrate crystallized on addition of acetone (Found on recrystallized material : Pt, 30·3 ; H_2O, 8·4%. Calc. for $[Pt(C_5H_5N)_4]Cl_2.3H_2O$: Pt, 30·7 ; H_2O, 8·5%). The dry compound gradually lost pyridine at room temperature. The perchlorate was obtained by the addition of perchloric acid to a cold saturated solution of the chloride. The perchlorate was recrystallized twice from hot water and dried at 100 °C (Found : Pt, 27·6%. Calc. for $[Pt(C_5H_5N)_4](ClO_4)_2$: Pt, 27·5%). No loss of pyridine from this compound was detected.

(vi) cis-*Dipyridinediammineplatinum(II) Perchlorate.* *cis*-Dichlorodiammineplatinum(II) was prepared by the slow drop-wise addition of dilute NH_3 to a warm solution of potassium tetrachloroplatinate(II). Recrystallization from hot water yielded a yellow crystalline material (Found : Pt, 64·7%. Calc. for $[Pt(NH_3)_2Cl_2]$: Pt, 65·0%). It dissolved readily in aqueous pyridine with gentle warming to yield a clear colourless solution from which sodium perchlorate precipitated well-formed colourless prisms. The perchlorate was recrystallized twice from hot water (Found : Pt, 33·3%. Calc. for $[Pt(NH_3)_2(C_5H_5N)_2](ClO_4)_2$: Pt, 33·3%).

(vii) trans-*Dipyridinediammineplatinum(II) Perchlorate.* *trans*-Dichlorodiammineplatinum(II), prepared by digesting at the boiling point a solution of tetrammineplatinum(II) chloride and HCl, was suspended in aqueous pyridine and heated on a steam-bath until a clear colourless solution was obtained. On cooling and adding sodium perchlorate, colourless prisms of *trans*-dipyridinediammineplatinum(II) perchlorate precipitated. The perchlorate was recrystallized twice from hot water (Found: Pt, 33·3%. Calc. for $[Pt(NH_3)_2(C_5H_5N)_2](ClO_4)_2$: Pt, 33·3%).

(viii) *Tripyridineammineplatinum(II) Perchlorate.* *cis*-Dipyridinediammineplatinum(II) chloride when heated in aqueous solution with HCl, decomposed to yield golden yellow crystals of dichloropyridineammineplatinum(II) by *trans*-elimination of one ammonia and one pyridine group. The yellow crystals were recrystallized from hot water (Found: Pt, 54·3%. Calc. for $[Pt(NH_3)(C_5H_5N)Cl_2]$: Pt, 53·9%). This compound was suspended in aqueous pyridine at room temperature for 12 hr with occasional stirring. From the clear colourless solution acetone precipitated a white crystalline material, which was dissolved in water, and the perchlorate precipitated by the addition of perchloric acid as colourless well-formed hexagonal prisms. The compound was recrystallized twice from hot water and dried at 100 °C (Found: Pt, 30·0%. Calc. for $[Pt(NH_3)(C_5H_5N)_3](ClO_4)_2$: Pt, 30·1%).

When the diammine was moistened with water and a slight excess of pyridine added, the reaction was quite fast at room temperature but stopped at the intermediate stage owing to the precipitation of the chlorotriammine compound as fine white needles. It was recrystallized from water (Found: Pt, 42·0%. Calc. for $[Pt(NH_3)(C_5H_5N)_2Cl]Cl$: Pt, 42·5%). The chloride was converted to the perchlorate by means of aqueous perchloric acid and recrystallized from water forming lustrous plates (Found: Pt, 38·8%. Calc. for $[Pt(NH_3)(C_5H_5N)_2Cl]ClO_4$: Pt, 38·6%).

When the chlorotriammine was dissolved in dilute aqueous pyridine and allowed to stand overnight, the mixed tetrammine was isolated from the solution.

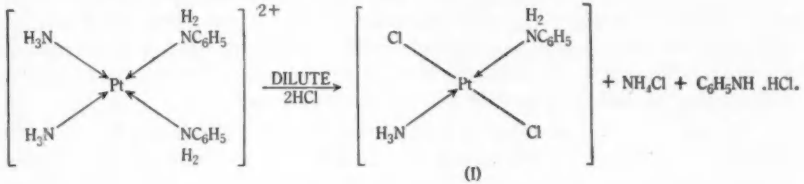
(ix) *Pyridinetriammineplatinum(II) Perchlorate.* *trans* - Dichloropyridineammineplatinum(II) was warmed with dilute aqueous NH_3. The yellow diammine dissolved readily. The addition of concentrated sodium perchlorate solution precipitated a white crystalline perchlorate, which was recrystallized twice from hot water (Found: Pt, 37·2%. Calc. for $[Pt(NH_3)_3(C_5H_5N)](ClO_4)_2$: Pt, 37·2%).

(x) cis - *Dianilinediammineplatinum(II) Perchlorate.* *cis*- and *trans*-dianilinediammineplatinum(II) chlorides are listed by Mellor (1937) as being prepared by P. T. Cleve. There appears to be no recent preparation of these tetrammines, but the following methods have been found suitable for the preparation of the corresponding perchlorates.

cis-Dichlorodiammineplatinum(II) was heated with water, and gradual additions of aniline were made, sufficient to keep the hot solution saturated with aniline. The hot solution was filtered to remove small amounts of tar. The chloride was precipitated by addition of ethanol-ether to the cooled solution. This was converted to the sparingly soluble perchlorate by dissolving in the

minimum amount of water and adding perchloric acid. The compound was recrystallized twice from hot water to yield pearly-white hexagonal plates (Found: Pt, 31·9; N, 9·1%. Calc. for $[Pt(NH_3)_2(C_6H_5NH_2)_2](ClO_4)_2$: Pt, 31·8; N, 9·1%).

When digested with hot dilute HCl this compound yielded greenish yellow needles of dichloroanilineammineplatinum(II), sparingly soluble in cold water. (Found: Pt, 51·8%. Calc. for $[Pt(NH_3)(C_6H_5NH_2)Cl_2]$: Pt, 51·9%). The reaction with HCl proceeded by *trans*-elimination of one ammonia and one aniline group according to the equation

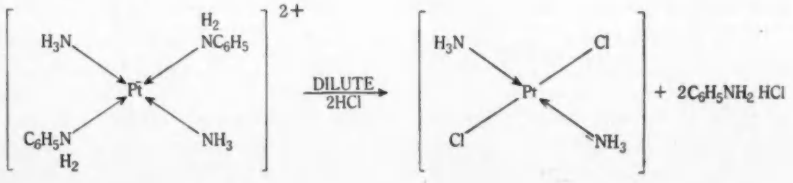


(I)

Attempts to dissolve I in aqueous aniline or NH_3 solution to yield the corresponding triammines were unsuccessful.

(xi) trans - *Dianilinediammineplatinum(II) Perchlorate.* *trans* - Dichlorodiammineplatinum(II) was prepared by action of hot dilute HCl on tetrammineplatinum(II) chloride. The sparingly soluble diammine was heated with aqueous aniline to produce a clear solution from which sodium perchlorate precipitated greenish yellow crystals. This compound was repeatedly crystallized from hot water and charcoal and was finally obtained as well-formed yellow crystals consisting of square plates. On keeping in a desiccator the colour changed, without loss in weight, to chamois. Subsequent preparations of this compound yielded chamois coloured crystals directly from solution (Found: Pt, 31·6; N, 9·2%. Calc. for $[Pt(NH_3)_2(C_6H_5NH_2)_2](ClO_4)_2$: Pt, 31·8; N, 9·1%).

trans-Dianilinediammineplatinum(II) ion was more reactive with HCl than the *cis*-isomer. The former ion reacted rapidly with HCl to give dichlorodiammineplatinum(II) *exclusively*. The tetrammine (28·8 mg), warmed with dilute HCl, gave 10·9 mg of pale yellow crystals (theoretical yield, 14·1 mg) soluble in hot water and sparingly soluble in cold (Found: Pt, 65·0%. Calc. for $[Pt(NH_3)_2Cl_2]$: Pt, 65·0%). The reaction with HCl therefore takes place according to the equation



This reaction is contrary to that between HCl and *trans*-dipyridinediammine-platinum(II) ion. Drew *et al.* (1932, p. 1011) showed that this ion reacted with HCl to give a mixture of dichlorodipyridineplatinum(II) and dichlorodiammine-platinum(II). The proportions were dependent on the acid concentration, but invariably the dipyridine compound predominated.

(xii) *Attempted Preparation of Tetrakis(trimethylamine)platinum(II) Chloride.* The reaction between potassium tetrachloroplatinate(II), trimethylamine hydrochloride, and trimethylamine was very slow. A dilute solution of these reagents on standing at room temperature gradually deposited a small quantity of yellow crystals, presumably dichlorobis(trimethylamine)platinum(II), and large amounts of black metallic platinum, often in the form of a mirror. Attempts to recrystallize the yellow crystals produced further quantities of platinum. The yellow crystals appeared to be unreactive towards cold aqueous trimethylamine and on warming produced metallic platinum.

It was considered that tetrakis(trimethylamine)platinum(II) chloride cannot be prepared by conventional methods. Models indicate that there would probably be considerable steric hindrance involved in the formation of the tetrakis(trimethylamine)platinum(II) ion.

(xiii) *Attempted Preparation of Tetranilineplatinum(II) Chloride.* The preparation of this compound has been attributed to Raewsky (1848) by Mellor (1937). Examination of the original publication casts considerable doubt as to whether the compound was obtained. In the present work, *cis*-dichlorodianiline-platinum(II) was prepared as very insoluble pale buff coloured crystals, by the action of aqueous aniline on a solution of potassium tetrachloroplatinate(II). This compound appeared to be insoluble in aqueous alinine under all conditions.

III. Results and Discussion

All the complex ions were studied in potassium chloride as supporting electrolyte. Figure 1 shows the discharges occurring, together with the curve for potassium chloride.

It has been postulated previously that the continuous discharge occurring in the presence of platinum compounds is due to the formation of hydrogen from the electrolysis of water molecules (Hall and Plowman 1955*a*). A film of metallic platinum formed on the mercury surface by the electroreduction of the complex catalyses the reaction.

Figure 2 records the effect of gelatin on the discharges illustrated in Figure 1. It has been shown previously (Laitinen *et al.* 1948) that gelatin can cause a shift of the polarographic wave to more negative potentials. In the present case some of the shifts due to gelatin were actually to more positive potentials.

An examination of the Figures 1 and 2 indicates that in the reduction of *trans*-$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$, *cis*-$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$, and $[Pt(C_5H_5N)_4]^{2+}$, maxima had occurred and were effectively suppressed by gelatin. The reduction of these three ions yields a limiting current approximately equal to 2·7 μA. This current is of the order expected for a 2-electron change using a capillary with the reported characteristics (Hall and Plowman 1955*a*, p. 162). Hence

the electrode reactions, which were found from the log plots to be irreversible, may be represented by

$$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}+2e^-\rightarrow Pt+2NH_3+2C_6H_5NH_2, \quad .. \quad (1)$$

and

$$[Pt(C_5H_5N)_4]^{2+}+2e^-\rightarrow Pt+4C_5H_5N. \quad ..... \quad (2)$$

The discharge due to hydrogen formation, occurring after the limiting current region, may be represented by

$$Pt+H_2O+e^-\rightarrow Pt+\tfrac{1}{2}H_2+OH^-. \quad ..... \quad (3)$$

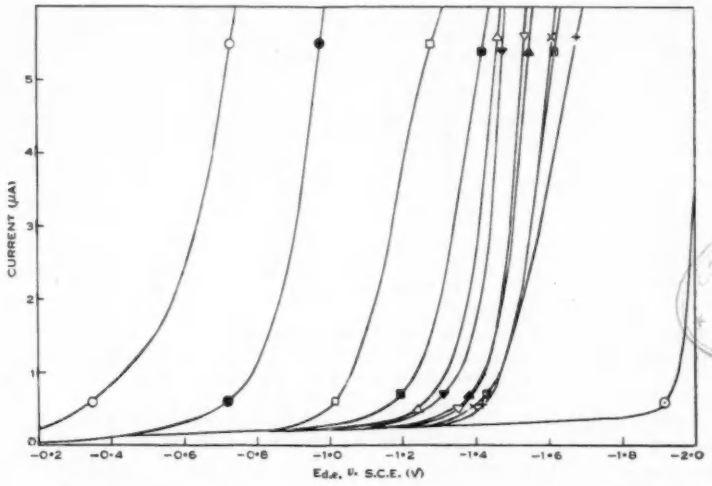


Fig. 1.—Current-voltage curves of the complex ions at a concentration equal to 0·5 mM, with supporting electrolyte 0·1M KCl. The key to the curves is set out in Table 1.

In the case of those ions which do not yield limiting current regions because of the interference of hydrogen formation, the electrode reactions which occur together may be represented in general by

$$\left.\begin{aligned}[Pt A_4]^{2+}+2e^-&\rightarrow Pt+4A,\\ Pt+H_2O+e^-&\rightarrow Pt+\tfrac{1}{2}H_2+OH^-.\end{aligned}\right\} \quad ..... \quad (4)$$

The magnitude of the displacement of the curves when gelatin is added is not the same for each species (even when the displacement is in the same direction); hence the order of reduction is different from that when gelatin is absent. It is conceivable that in the absence of gelatin other ions may reduce initially with a maximum, but that the formation of hydrogen interferes with the maximum before it can be completed. If gelatin were to suppress the maximum then the decomposition voltage of the ions would be appreciably affected. Such is probably the case with the reduction of $[Pt\,en_2]^{2+}$ where the shift amounts to 55 mV to more negative potentials.

Maximum suppression cannot account for the positive shift of the wave in the presence of gelatin. This fact amounts to easier reduction of the complex when gelatin is present.

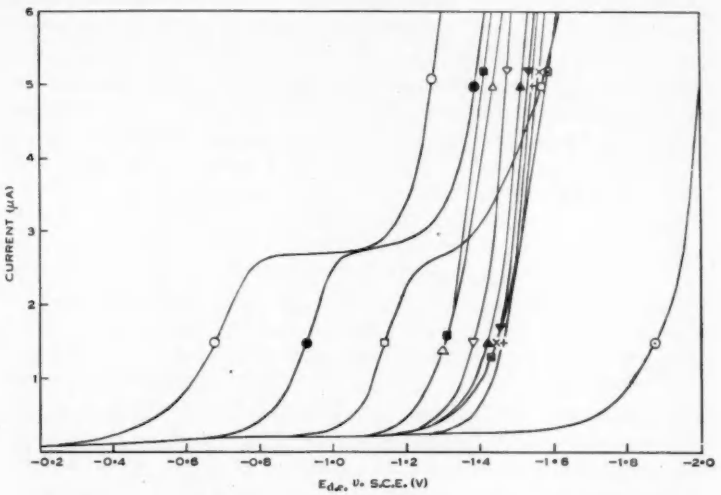


Fig. 2.—Current-voltage curves of the complex ions at a concentration equal to 0·5 mM, with supporting electrolyte 0·1 M KCl, 0·01 per cent. gelatin. The key to the curves is set out in Table 1.

Table 1 presents the ions in order of decreasing ease of reduction in 0·1 M KCl and 0·01 per cent. gelatin. Column 5 indicates the effect of gelatin. The positive sign denotes a shift to more positive voltages.

TABLE 1

POLAROGRAPHIC REDUCTION OF THE IONS IN 0·1M KCl AND 0·01 PER CENT. GELATIN

Symbol†	Ion	$E_{\frac{1}{2}}$ v. S.C.E. (V)	E^* v. S.C.E. (V)	Shift Caused by Gelatin (mV)
○	*trans*-$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$	−0·670	−0·670	−165
●	*cis*-$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$	−0·930	−0·922	− 90
□	$[Pt(C_5H_5N)_4]^{2+}$	−1·130	−1·135	− 45
■	$[Pt(NH_3)(C_5H_5N)_3]^{2+}$		−1·298	− 25
△	$[Pt(CH_3NH_2)_4]^{2+}$		−1·298	+ 50
▽	*trans*-$[Pt(NH_3)_2(C_5H_5N)_2]^{2+}$		−1·378	+ 70
▲	*cis*-$[Pt(NH_3)_2(C_5H_5N)_2]^{2+}$		−1·416	+ 35
▼	$[Pt\{C_2H_4(NH_2)_2\}_2]^{2+}$		−1·440	− 55
×	$[Pt(NH_3)_3(C_5H_5N)]^{2+}$		−1·440	+ 50
⊠	$[Pt(NH_3)_4]^{2+}$		−1·440	+ 50
+	$[Pt\{(CH_3)_2NH\}_4]^{2+}$		−1·460	+ 40
⊙	K^+			

† These symbols also form the key to the curves, Figures 1–4.

It was necessary to decide upon some method by means of which the order of reduction of the ions could be measured. The 45° tangent method (decomposition potential) was dispensed with because of the dissimilar slopes of the curves in the early stages of the reductions.

If hydrogen formation did not interfere with the reduction of the ions, then it would be reasonable to expect a series of 2-electron waves whose half-wave potentials were characteristic of the ionic species undergoing the particular reduction. It appeared that a better comparison could be obtained if voltages were measured corresponding to a current approximately equal to one-half of that expected for a 2-electron change of a similar ion.

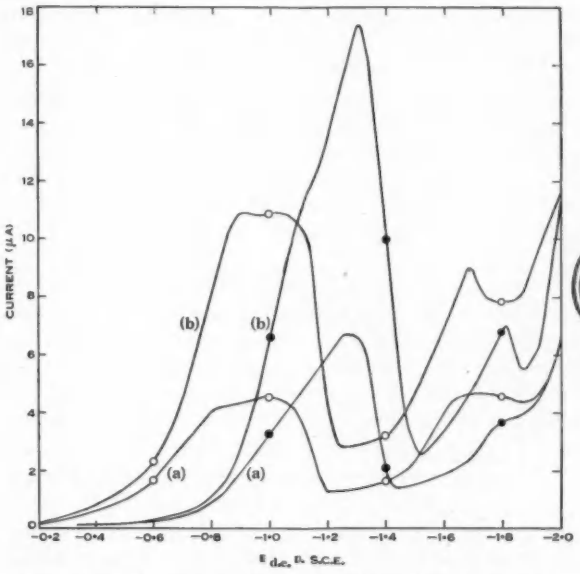


Fig. 3.—Complete current-voltage curves of the *cis*- and *trans*-isomers of $[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$ at concentrations equal to (*a*) 0·25 mM, (*b*) 0·50 mM, in 0·1 M KCl.

The half-wave potential for *trans*-$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$ occurred at a current equal to 1·40 μA. This value was used as an arbitrary standard for measurement of the approximate half-wave voltages. Table 1 lists the values of E^*, the voltage corresponding to 1·40 μA for the remaining curves.

Figure 3 shows the complete c-v curves of the *cis*- and *trans*-isomers of $[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$. The dependence of current on concentration is illustrated.

The reduction of each ion exhibits a maximum after which the current decreases rapidly to the region of the diffusion current. The current increases again to a maximum, usually not as high as the first, followed by a sensibly

constant current section before discharge of potassium ions at *c.* $-1 \cdot 9$ V *v.* S.C.E. The second plateau falls about $-1 \cdot 8$ V *v.* S.C.E. and is considered due to the formation of hydrogen which is limited by the quantity of metallic platinum produced (Slendyk and Herasymenko 1932). The currents recorded in the curves between the two maxima are only approximate, as consistent oscillations of the galvanometer spot were not obtainable for a fixed voltage setting. Just as the limiting currents of some of the ions cannot be realized before the interference by hydrogen formation, so the limiting current of hydrogen formation, as evident in Figure 3, may not be realized before potassium ions begin to discharge. This is so, for example, in the reduction of $[Pt(NH_3)_4]^{2+}$.

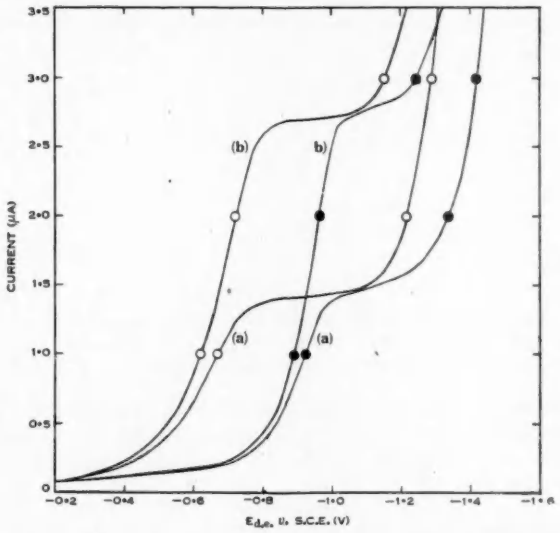


Fig. 4.—Current-voltage curves of the *cis-* and *trans*-isomers of $[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$ at concentrations equal to (*a*) 0·25 mM, (*b*) 0·50 mM, in 0·1 M KCl and 0·01 per cent. gelatin.

The proportionality between diffusion current and concentration is more readily observed from Figure 4 which shows the reduction of the isomers at the concentrations 0·25, 0·50 M in 0·1 M KCl, and 0·01% gelatin. Here again the second discharge represents hydrogen formation but the limiting current reached in this case was about three times that in the absence of gelatin. Further, the hydrogen wave starts at a voltage more positive by *c.* 0·2 V than in the absence of gelatin.

It has been shown with coordination compounds of cobalt(III) (Willis, Friend, and Mellor 1945; Holtzclaw 1951; Holtzclaw and Sheetz 1953) that the *cis*-isomer was more readily reducible than the *trans*- when the six ligands comprised two electronegative groups and four neutral groups. Isomeric complexes without electronegative groups exhibited no such difference.

In the case of the four-covalent platinum complexes two variations from the above results are apparent. Firstly, the distinction between the *cis*- and *trans*-forms occurs in the absence of electronegative groups. Secondly, it is the *trans*-isomer which is reduced more readily. The experimental results reported by Holtzclaw and Sheetz (loc. cit.) show easier reduction of the *trans*-isomer for the case of cobalt(III) complexes containing one electronegative and five neutral groups.

It is to be noted that extensive separation of the c-v curves of *cis*- and *trans*-isomers occurs when the bond strengths of the two different ligands are obviously greatly at variance. This is especially so in the case of the ammonia-aniline isomers. Further, all the ions obtained by replacing, one at a time, the ammonia groups in $[Pt(NH_3)_4]^{2+}$ by pyridine groups, yield c-v curves which progressively shift to more positive voltages. Consequently, $[Pt(C_5H_5N)_4]^{2+}$ is reduced at the most positive voltage of the series.

Therefore in order to distinguish between isomers of the type $[PtA_2B_2]^{2+}$, it is probably necessary for the ligands A, B, to differ significantly in the strength of their coordinate bonds to platinum. The difference in bond strength between Pt-A and Pt-B must be sufficient to result in a reasonable separation of the c-v curves of $[PtA_4]^{2+}$ and $[PtB_4]^{2+}$. Hence, a polarographic distinction between the *cis*- and *trans*-isomers of $[Pt(NH_3)_2\{(CH_3)_2NH\}_2]^{2+}$ would probably be undetectable.

The more facile reduction of the *trans*-isomer of $[PtA_2B_2]^{2+}$ would possibly indicate that this isomer is thermodynamically less stable than the *cis*. Chatt and Wilkins (1952) found the *cis*-isomer of $[(PEt_3)_2PtCl_2]$ to be more stable than the *trans*. These authors report a difference in heat content equal to 10 kcal. The authors conclude that the greater stability of the *cis*-isomer may be due to π-bonding through *d*-orbitals in the phosphorus and platinum atoms. This explanation, using π-bonding, cannot be applied in the case of the isomers of $[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$.

It is to be noted than *trans*-$[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$ reacts very readily with HCl to produce *trans*-$[Pt(NH_3)_2Cl_2]$ exclusively. The *cis*-isomer reacts slowly with HCl to produce the mixed diammine $[Pt(NH_3)(C_6H_5NH_2)Cl_2]$.

HCl does not react with the *trans*-isomer of $[Pt(NH_3)_2(C_5H_5N)_2]^{2+}$ in the same way. Drew *et al.* (1932, p. 1011) reported that *trans*-$[Pt(NH_3)_2(C_5H_5N)_2]^{2+}$, on reaction with HCl, did not yield the two *trans*-dichlorodiammines in equal proportions but the proportion of *trans*-$[Pt(C_5H_5N)_2Cl_2]$ was greater.

A difference in reactivity of *cis*- and *trans*-diammines is mentioned by Syrkin (1948). The *trans*-dichlorodiammineplatinum(II) reacts much more readily with $AgNO_3$ than the *cis*-isomer. This is explained by Syrkin on the ground of paired bonds. Syrkin postulates that the ligand which is most covalently bound increases the degree of covalency of the bonds in the *cis*-positions and labilizes the group in the position *trans* to it.

A difference in behaviour of the mixed aniline-ammonia and the mixed pyridine-ammonia compounds with HCl is probably accounted for by the much greater difference in bond strengths where aniline is concerned. In the case of

the isomers of $[Pt(NH_3)_2(C_6H_5NH_2)_2]^{2+}$, the first step in the course of the reaction with HCl may be the replacement of one aniline by chlorine. Then, in the *cis*-isomer the remaining aniline group is strengthened and the *trans*-NH_3 group is labilized, leading to the formation of the mixed diammine, *trans*-dichloro-anilineammineplatinum(II). In the case of the *trans*-isomer, the chlorine which replaces an aniline group immediately labilizes the remaining aniline which is *trans* to it. Hence, *trans*-dichlorodiammineplatinum(II) is formed rapidly.

IV. Acknowledgments

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THE PHOTOLYSIS OF GASEOUS ALDEHYDES

I. THE PRODUCTION OF ETHANE AND HYDROGEN IN THE PHOTOLYSIS OF ACETALDEHYDE

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Summary

The rate of production of ethane in acetaldehyde photolysis has been calculated from iodine-methyl trapping experiments, and compared with the experimental values over the temperature range 120–360 °C. The ratio of observed to calculated ethane rises from 0·5 at 120 °C to 2 at 350 °C, whilst the ratio of observed hydrogen to observed ethane rises from 0·25 at 120 °C to 1 at about 300 °C. The activation energy using the methyl radical concentration was calculated to be 7·4 kcal mole^{-1} for the reaction

$$CH_3+CH_3CHO \rightarrow CH_4+CH_3CO.$$

It was concluded that formyl radical recombination occurred in a higher temperature region (up to about 300 °C) than acetyl radical recombination (up to about 200 °C) for the experimental conditions used. It was also found that in the temperature region above about 250 °C a significant hydrogen atom chain initiation occurred.

I. INTRODUCTION

This investigation is a continuation of that of Danby, Buchanan, and Henderson (1951) and Buchanan (1951). In these two papers it was concluded, on the basis of mass-spectrometric analysis for ethane and hydrogen and comparison of the observed with calculated ethane (the latter being computed from the rate of production of methyl radicals as determined by trapping with iodine), that the following reaction mechanism was probable in the temperature range 200–350 °C:

$$CH_3CHO \xrightarrow{h\nu} CH_3+CHO, \quad \ldots\ldots\ldots\ldots (1)$$

$$CH_3+CH_3CHO \longrightarrow CH_4+CH_3CO, \quad \ldots\ldots\ldots\ldots (2)$$

$$CH_3CO \longrightarrow CH_3+CO, \quad \ldots\ldots\ldots\ldots (3)$$

$$HCO \longrightarrow H+CO, \quad \ldots\ldots\ldots\ldots (4)$$

$$2CH_3 \longrightarrow C_2H_6, \quad \ldots\ldots\ldots\ldots (5)$$

$$H+CH_3CHO \longrightarrow H_2+CH_3CO, \quad \ldots\ldots\ldots\ldots (6)$$

$$2H(+M) \longrightarrow H_2(+M). \quad \ldots\ldots\ldots\ldots (7)$$

An increase in the ratio of observed to calculated ethane from ~1 at 210 °C to ~2 at 350 °C was taken as evidence for reactions (4) and (6) since formyl radicals are here effectively converted to methyl radicals which eventually combine to give ethane. Approximate equality of ethane and hydrogen, as was found experimentally, is consistent with this mechanism.

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The logical extension of the investigation is to the temperature region between 100 and 200 °C, where chain decomposition represented by reactions (**2**) and (**3**) becomes important. It is desirable to establish the factors responsible for the transition: in this respect the stability of the radicals formyl, and in particular acetyl, seems to be significant, since either or both reactions (**2**) or (**3**) must be critical in determining the onset of the chain reaction. We therefore sought evidence as to whether (i) the ratio of observed to calculated ethane remained at unity in the range 100–200 °C, that is, whether all the primary methyl radicals gave ethane, and (ii) whether the ratio of hydrogen to ethane remained at unity, that is, whether glyoxal formation followed upon increasing stability of the formyl radical.

The validity of using iodine trapping as a means of determining the rate of production of methyl radicals has been questioned by Steacie and Lossing (1953) on the grounds that (as reported in the earlier work) the experimentally observed ethane was in excess of that calculated from the rate of formation of methyl radicals determined by iodine trapping. Steacie and Lossing suggest that the difference may have been due to iodine deactivation of excited CH_3CHO molecules. However, in fact, the ratio of observed to calculated ethane is unity at about 200 °C, and increases towards two as the temperature rises. As we and other authors (Blacet and Loeffler 1942; Benson and Forbes 1943; Pitts and Blacet 1952) have demonstrated, the iodine traps the primary methyl radicals so effectively that reactions (**2**) and (**3**) are completely suppressed. Similarly the formyl radicals in the presence of iodine give hydrogen iodide which appears to be trapped in aldehyde polymer and therefore cannot be determined. The ratio of observed to calculated ethane should eventually reach two when all of the formyl radicals decompose at higher temperatures and each resultant H atom produces a methyl radical by way of reaction (**6**).

As a further means of investigating the chain decomposition of acetaldehyde, we observed rates of reactions with mixtures containing acetone, formaldehyde, biacetyl, and glyoxal. These results and their correlation with the data of the present paper are discussed in Parts III and IV of this series (Dorman and Buchanan 1956*a*, 1956*b*).

II. Experimental and Results

(*a*) *Trapping of Methyl Radicals with Iodine*

The apparatus used differed a little from that previously described (Buchanan 1951), although the procedure was almost the same. The acetaldehyde, from three different sources, namely, B.D.H. redistilled in nitrogen, ethyl alcohol oxidation, paraldehyde depolymerization, and with or without final addition of recrystallized hydroquinone to the storage vessel, gave identical results in each case. Irradiation of the silica reaction vessel (length 10 cm, radius 1·5 cm), placed in a furnace held at 200 ±2 °C, was by a 125 W medium pressure mercury arc. The calculated aldehyde absorption was about 60 per cent. of the 3130 and 3020 lines and about 30 per cent. of the 2800 and 2650 lines. After vapourizing the weighed iodine (2–10 mg ≡ 0·4–1·8 cm Hg pressure) previously stored over P_2O_5, into the reaction vessel, adding the acetaldehyde, and irradiating for 5 or 10 min, the products were pumped slowly past mercury absorption

U-tubes at room temperature and the methyl iodide and excess aldehyde collected in sodium ethylate at −80 °C. The sodium iodide from the methyl iodide was then determined volumetrically using N/80 $Na_2S_2O_3$ either after standing for 1 hr (0·1 c.c. blank) or heating at 130 °C for 1 hr. The analytical procedure was checked with a methyl iodide-alcohol solution of known concentration.

Blank runs, omitting only the actual irradiation, demonstrated that small amounts of iodoacetaldehyde polymer, always present, were not reaching the sodium ethylate. The production of CH_3I for irradiation times of 5 and 10 min is shown in Figure 1. The aldehyde pressure was corrected for iodine partial pressure, but no arc deterioration corrections were required, as shown by separate rate experiments. The results were found to be independent of iodine pressure, at least within the limits quoted above, which always represented excess of

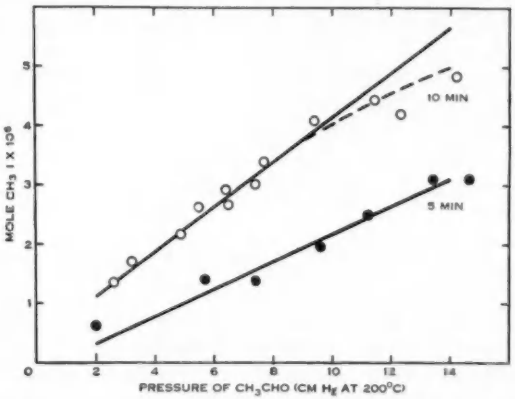

Fig. 1.—Production of CH_3I in the photolysis of mixtures of CH_3CHO and I_2.

iodine. The curves of CH_3I yield *v.* CH_3CHO pressure were linear up to about 10 cm Hg pressure for the 10 min runs and to about 15 cm Hg pressure for the 5 min runs, becoming non-linear above these pressures. The straight lines were used to give the rate of production of methyl radicals and hence to enable calculation of ethane production as described previously (Buchanan 1951).

Attempts to find hydrogen iodide by condensing the contents of the reaction vessel to −183 °C were not successful, although the erratic results indicated the formation of a moderately volatile iodoaldehyde polymer. It was concluded, in agreement with earlier findings (Blacet and Loeffler 1942), that hydrogen iodide is lost and that the iodine experiments give only the methyl radical production.

(*b*) *Ethane and Hydrogen Gas Analysis*

After irradiating 10 cm Hg of acetaldehyde with the full arc for 20 min at 120 °C, 5 min at 200 °C, etc. to give 5–10 per cent. decomposition, the excess aldehyde was removed with moist sodium bisulphite dispersed on glass tubes contained in a U-tube. The bisulphite tube was then frozen to −80 °C and

the residual gases, CH_4, CO, C_2H_6, H_2, and also a trace of air from the bisulphite were collected. No water, air, or SO_2 from the bisulphite absorber was allowed to reach the reaction vessel. The walls of the reaction vessel were brought to a reproducible condition by carrying out several runs with illumination and discarding the products. Presumably this procedure removed adsorbed air or water. The collected gases were analysed for CH_4, CO, C_2H_6, and H_2 using a Consolidated Engineering Corp. 180° type 21–102 mass spectrometer with photographic recording. The analyses were performed by Dr. A. J. C. Nicholson, C.S.I.R.O., to whom the authors wish to express their thanks for this assistance. The mass spectrometer was calibrated for the above gases and duplicate runs at 205 °C gave close agreement.

Below 250 °C lines 26, 27, and 30 agreed well for the ethane, but above 250 °C the peak heights were small (hence the accuracy was low owing to background corrections), and line 30 gave lower results whilst lines 26 and 27 still agreed. We have used the average of lines 26 and 30. Line 30 was corrected for $^{12}C^{18}O$ assuming the ^{12}C to ^{13}C ratio to be the same as in the calibration CO. Line 2 with separate focusing was used for hydrogen. The relative observed percentage (Table 1) is for equal amounts of gas produced (mainly CH_4 and CO) from equal initial amounts of acetaldehyde (10 cm Hg pressure at 200 °C). The results obtained are presented in Table 1 and Figure 2.

TABLE 1

PRODUCT ANALYSIS IN ACETALDEHYDE PHOTOLYSIS

Temp. (°C)	Relative $\frac{H_2}{C_2H_6}$ (%)	Observed $\frac{H_2}{C_2H_6}$ (%)	Hydrogen / Ethane	"Calculated" Ethane (%)	Observed / Calculated Ethane	Methane / Ethane	Carbon Monoxide / Methane
120	0·55	2·00	0·28	4·16	0·48	24·9	0·96
150	0·68	2·00	0·34	3·78	0·53	25·3	0·92
180	1·13	2·30	0·48	3·30	0·70	21·0	1·03
205	1·47	2·90	0·50	3·00	0·97	16·7	1·02
205	1·46	3·00	0·50	3·15	0·95	15·9	1·05
255	2·40	3·30	0·70	2·60	1·30	14·6	0·95
305	3·14	3·20	1·00	2·20	1·50	14·6	1·03
365	—	3·50	—	1·70	2·00	13·5	0·97

III. DISCUSSION

Having in mind the mechanism given above, we interpret the ratios of Table 1 and Figure 2 as follows. The hydrogen-ethane ratio should become unity when all of the initial formyl radicals undergo decomposition (reaction (4)) and produce molecular hydrogen by reaction (6), and possibly reaction (7), occurring at the wall. Each H atom from (4) gives a methyl radical by (6) and recombination of these methyls to give ethane should then maintain equality between hydrogen and ethane. Since this condition is reached at a temperature somewhat above 300 °C (Fig. 2), it is likely that all of the formyls are decomposing at this temperature.

The higher the proportion of formyl radicals giving ethane by reactions (4) and (6), the closer should the ratio of observed to calculated ethane approach to two, since CH_3 and CHO are produced in equal amounts initially. This condition is reached at a temperature somewhat above 300 °C, and to within the limits of our experimental accuracy, at approximately the same temperature as H_2/C_2H_6 becomes unity. Hence we infer that at this temperature all the formyls decompose to give H atoms which yield H_2 by reaction (6). Reaction (7) appears to be *absent*, an important conclusion since it permits us to postulate other reactions to account for the H_2 produced in the low temperature photolysis. The absence of (7) in any case appears probable since (6) is likely to be a fast reaction and the concentration of CH_3CHO is of course high, relative to the radical concentration. Values of the hydrogen-ethane ratio below unity must be explained as due in part at least to combination of formyl radicals to give glyoxal, a reaction which we therefore add to the suggested mechanism below 300 °C.

When the observed to calculated ethane ratios becomes unity at ~200 °C, only the primary methyl radicals are leading to ethane, and reaction (6) must be absent because of inappreciable formyl decomposition and hence low H atom concentration. If (6) and hence (4) are absent, then we are left with no reactions producing molecular hydrogen and yet, experimentally, the ratio of hydrogen to ethane is 0·5 at this temperature. We therefore suggest the reactions

$$HCO \rightarrow \tfrac{1}{2}H_2 + CO, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (8)$$

$$2HCO \rightarrow H_2 + 2CO, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (8a)$$

as the most probable means of producing the required hydrogen. Reaction (8) is to be preferred to (8a) by analogy with H atom combination which is more likely to occur at the wall than in the gas phase. There is no reason to suppose that reaction (8) is not operative at higher temperatures, although here H atoms are less likely to remain adsorbed on the wall and combine to molecular hydrogen. Major competition to reactions (8) and (8a) will come from the gas phase decomposition of formyl radicals, negligible at 120 °C, but, because of the high energy of activation (20–25 kcal $mole^{-1}$, see below), accounting for most of the formyl radicals above 300 °C.

As Figure 2 shows, the hydrogen-ethane ratio decreases to 0·25 at 120 °C and, since ethane production is decreasing on dropping from 200 to 120 °C, we infer that the proportion of formyl radicals undergoing reactions (8) and (8a) to give hydrogen is diminishing, presumably glyoxal formation consuming a progressively greater proportion.

As the reaction temperature drops below 200 °C, the value of observed to calculated ethane becomes less than unity, reaching 0·5 at 120 °C, a result which must be due to loss of primary methyl radicals in radical-radical reactions of the following kind:

$$CH_3 + CH_3CO \rightarrow CH_3COCH_3 \text{ (Volman and Brinton 1952)}, \ldots\ldots (9)$$

$$2CH_3CO \rightarrow (CH_3CO)_2 \text{ (Blacet and Blaedel 1940)}, \ldots\ldots (10)$$

$$CH_3 + CHO \rightarrow CH_4 + CO \text{ (Leermakers 1934)}. \ldots\ldots\ldots (11)$$

Reactions (**9**) and (**10**) seem most probable at these low temperatures; they would of course disappear above 200 °C because of the low concentration of acetyl radicals. Reaction (**11**) is not favoured, principally because if it occurred

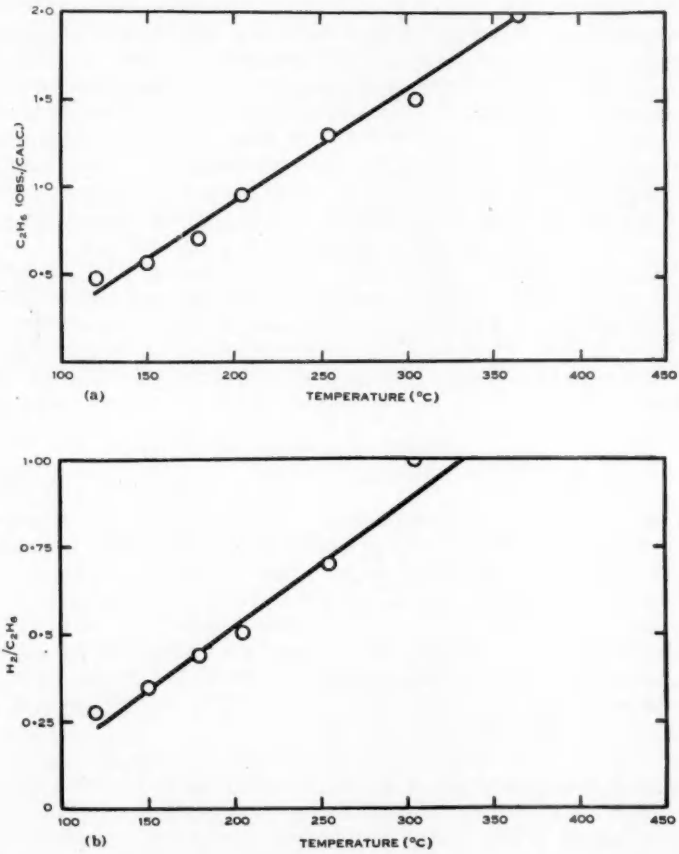

Fig. 2.—Variation with temperature of (*a*) the ratio of observed to calculated ethane and (*b*) the ratio of hydrogen to ethane, in the photolysis of acetaldehyde.

at 120 °C it should also be present above 200 °C, and yet ethane formation appears to be the only reaction for removing methyl radicals for which there is any evidence in the high temperature region, apart from a possible small wall loss to form methane.

In view of this discussion, and of further arguments given below, we propose to recast the reaction mechanism as follows:

Above 200 °C

$$CH_3CHO \xrightarrow{h\nu} CH_3 + CHO, \quad \ldots\ldots (1)$$

$$CH_3 + CH_3CHO \longrightarrow CH_4 + CH_3CO, \quad \ldots\ldots (2)$$

$$CH_3CO(+M) \longrightarrow CH_3 + CO(+M) \quad (p \geqslant \sim 10 \text{ cm Hg}), \quad \ldots\ldots (3)$$

$$HCO(+M) \longrightarrow H + CO(+M) \quad \text{(pressure dependent)}, \quad \ldots\ldots (4)$$

$$2CH_3 \longrightarrow C_2H_6, \quad \ldots\ldots (5)$$

$$CH_3 \xrightarrow{\text{wall}} \text{products} \quad (C_2H_6; CH_4) \quad \text{(small)} \quad \ldots\ldots (5a)$$

$$H + CH_3CHO \longrightarrow H_2 + CH_3CO, \quad \ldots\ldots (6)$$

$$2HCO \longrightarrow (HCO)_2 \quad \text{(below } \sim 300 \text{ °C)} \quad \ldots\ldots (7)$$

$$HCO \xrightarrow{\text{wall}} \tfrac{1}{2}H_2 + CO, \quad \ldots\ldots (8)$$

$$2HCO \longrightarrow H_2 + 2CO \quad \text{(small)}. \quad \ldots\ldots (8a)$$

Below about 200 °C we omit reaction (**6**) because of the low H atom concentration due to the absence of reaction (**4**). It is also necessary to consider the primary reaction

$$CH_3CHO \xrightarrow{h\nu} CH_4 + CO,$$

which will become more important at lower temperatures and shorter wavelengths (cf. Steacie and Lossing 1953). Reaction (**3**) probably diminishes whilst (**7**), (**8**), and (**8a**) become more important. The radical-radical reactions (**9**), (**10**), and (**11**) given above probably assume greater significance as the rate of decomposition of acetyl radicals diminishes. The light intensity would appear to determine the exact mechanism of the low temperature reaction. Low intensity should favour radical decomposition as compared with combination reactions, because of lower radical concentrations. An experimental search for glyoxal and diacetyl with varying light intensity and wall conditions is required to clarify these matters.

A theoretical discussion (see Dorman and Buchanan 1956*a*, Part II of this series), using Bawn's (1938) method with new parameters, gave $E_4 \simeq 25$ kcal mole^{-1} and $E_3 \simeq 15$ kcal mole^{-1}. Substituting these values for E_3 and E_4 in Benson's (1952) equation (**14**), we find pressure dependence for the formyl decomposition below several atmospheres pressure, and pressure dependence for the acetyl decomposition below 5–15 cm Hg pressure (see also Davis 1947).

In addition to the above data on the hydrogen and ethane ratios there are other grounds for believing that formyl radicals have sufficient stability up to about 300 °C to undergo reactions (**7**) and (**8**). A reconsideration of Calvert and Steacie's (1951) formaldehyde mechanism (Part III of this series) requires formyl combination to glyoxal, for near-zero activation energy, to have a rate of $\sim 10^{10}$ c.c. mole^{-1} sec^{-1}, and gives the wall decomposition of formyl as the main chain breaking step. Using this result and E_4 ~ 22 kcal mole^{-1}, the ratio of formyl decomposition to recombination at 220 °C is of the order of

10^{-2} ((HCO)$\simeq 10^{-10}$ mole c.c.$^{-1}$). Consequently recombination up to temperatures of 300 °C appears to be feasible.

The wall rates of radical loss calculated (cf. Shuler and Laidler 1949), using the experimental hydrogen atom rate of 10^3 sec^{-1} (Smith 1943), give methyl radical loss as $\sim$20 sec^{-1}, formyl radical loss as $\sim 0{\cdot}1$ sec^{-1}, and acetyl radical loss as $\sim 10^{-3}$ sec^{-1} at about 220 °C. It is therefore likely that reaction (**5a**) is small but not insignificant relative to (**5**). Both ethane and methane may be expected from methyl loss on the walls.

From the rate of production of ethane, known from the iodine trapping experiments, and the specific rates for reactions (**5**) and (**5a**), we can calculate the methyl radical concentration (i.e.

$$\frac{\mathrm{d}}{\mathrm{d}t}(\mathrm{C_2H_6}) = k_5(\mathrm{CH_3})^2 + \tfrac{1}{2}\alpha k_{5a}(\mathrm{CH_3}),$$

where α is an unknown constant $0 < \alpha \leqslant 1$). Assuming $k_5 \simeq 10^{13}$ sec^{-1} (Gomer and Kistiakowsky 1951) and $k_{5a} \simeq 20$ sec^{-1} (Shuler and Laidler 1949), then the methyl radical concentration is 10^{-12} mole c.c.$^{-1}$ for temperatures of about 220 °C. Making the further assumption that the overall rate of reaction is determined by the chain step (**2**), we have

$$\text{rate} = k_2(\mathrm{CH_3CHO})(\mathrm{CH_3})$$

and

$$E_2 = RT \ln A_2(\mathrm{CH_3CHO})(\mathrm{CH_3})/\text{rate},$$

where A_2 is the pre-exponential factor for reaction (**2**). Taking

$$A_2 = 4 \times 10^{10} T^{\frac{1}{2}} \text{ c.c. mole}^{-1} \text{ sec}^{-1} \text{ (Volman and Brinton 1952)},$$

we calculate that

$$E_2 = 7{\cdot}4 \text{ to } 7{\cdot}5 \text{ kcal mole}^{-1} \ (\alpha = 1{,}0) \text{ at } 220\ ^\circ\mathrm{C},$$

in agreement with Volman and Brinton's figure of $7{\cdot}5$ kcal mole^{-1}. High values of E_2 (about 10 kcal mole^{-1}) previously reported by Dodd (1953) would appear to be due to either too large a temperature range and hence a varying methyl radical concentration, or else an incorrect mechanism.

If we assume $S_2 \sim 10^{-3}$, where S_2 is the steric factor for reaction (**2**), and hence take A_2 as $\sim 10^{10}$–10^{11}, and $E_2 = 7{\cdot}4$ kcal mole^{-1}, then inversely we obtain $k_5 \sim 10^{13}$, which agrees with the theoretical discussion of Rollefson (1952) and Hill (1949) for the methyl radical recombination reaction.

(*a*) *The Chain Reaction in Acetaldehyde Photolysis*

Appreciable chain reaction begins in the temperature region of 160 to 180 °C. As stated above, reaction (**2**) has an energy of activation of about $7{\cdot}5$ kcal mole^{-1}, whilst reaction (**3**) has a value of 15 kcal mole^{-1}, and hence provided the frequency factors do not differ greatly we should expect increasing rate of decomposition of the acetyl radical to be principally responsible for the onset of chain reaction. Other arguments may be given to support this suggestion. The ratio of observed to calculated ethane falls below unity at temperatures

below about 200 °C (Fig. 2), a result interpreted as due to loss of primary methyl radicals because of increasing stability of the acetyl radical at lower temperatures (reactions (**9**) and (**10**)). In addition, there seems to be general agreement that reaction (**2**) is still effective at temperatures much below the chain limit of 160–180 °C (Steacie 1946). The analogous reaction to (**2**) in acetone photolysis yields methane and the CH_2COCH_3 radical in appreciable amount at 200 °C, and, since H atom abstraction is likely to be easier in acetaldehyde than in acetone, it seems probable that the absence of chain reaction in acetone photolysis is due to the relative stability of the CH_2COCH_3 radical. Conversely, the presence of chains in acetaldehyde photolysis is then due to the instability of the acetyl radical.

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THE PHOTOLYSIS OF GASEOUS ALDEHYDES

II. THE DECOMPOSITION OF FORMYL AND ACETYL RADICALS

By F. H. DORMAN* and A. S. BUCHANAN*

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Summary

The potential energy surfaces for the decomposition of HCO, CH_3CO, and COCl radicals have been constructed using Bawn's (1938, 1939) method with new parameter values. The values obtained for the energies of activation for decomposition were of the order of 26, 18, and 6 kcal $mole^{-1}$ respectively. The CH_3CO and COCl values agree with experimental estimates and consequently it is believed that the formyl value is of the correct order of magnitude.

I. INTRODUCTION

That it is possible to construct a unimolecular potential energy surface by superimposing a " collision " energy surface on a vibrational energy surface Bawn (1938, 1939) has shown. Generally, the accuracy is not high because of the simple collisional model that has to be used. In the present paper the aim has been to use consistent parameter values for the closely similar HCO, CH_3CO, and COCl decompositions, this comparative procedure being possible because of the existence of experimental estimates for the energies of activation of decomposition of the latter two radicals. The values obtained for formyl and acetyl have been shown in Parts I, III, and IV of this series (Dorman and Buchanan 1956*a*, 1956*b*, 1956*c*) to be in agreement with postulated mechanisms for the photolysis of acetaldehyde and formaldehyde (temp. >120 °C).

II. THE VIBRATIONAL SURFACE FOR THE MOLECULE R—C—O (SURFACE I)

This surface was constructed using the Morse curves for the diatomic molecules R—C and C—O. A family of R—C curves was prepared, each curve corresponding to a particular value of r_{C-O} and displaced from its neighbour by the energy required to stretch or compress the C—O bond (read from the CO Morse curve) over the appropriate distance. From this family of curves a series of values of the energy of the molecule R—C—O for pairs of values of r_{R-C} and r_{C-O} was obtained. Each pair of values of r_{R-C} and r_{C-O} was then plotted on a suitable graph, the energy of R—C—O corresponding to this point noted, and when sufficient points had been obtained, those of equal energy were connected by contour lines, thus giving the vibrational energy surface for the molecule.

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The Morse equation is of the form

$$U_{(r)}=D_e(1-e^{-2\beta\zeta})^2,$$

where

$$\zeta=\frac{r-r_e}{r_e},$$

r_e being the equilibrium internuclear distance, D_e the bond energy measured from the minimum of the potential energy curve, and β a constant given by

$$\frac{\omega_e}{4(B_eD_e)^{\frac{1}{2}}};$$

ω_e and B_e being vibrational and rotational constants respectively.

$$B_e=\frac{h}{(8\pi^2cI)},$$

where I is the moment of inertia, c the velocity of light, and h is Planck's constant. In order to prepare the Morse curves, we therefore require values for r_e, ω_e, and D_e for R—C and C—O in the molecule R—C—O. For acetyl and formyl these were assumed to be equal to or a little less than in the parent aldehyde (Table 1). Small variations in these parameters have small effects on the final E (energy of the crossing point) values. For example, $r_{H-C}=1{\cdot}13$ Å causes a decrease in E_c for HCO by $\sim\frac{1}{2}$ kcal mole^{-1}.

TABLE 1

PARAMETERS USED IN COMPUTING VIBRATIONAL SURFACES

Reaction	Bond	r_e (Å)	ω_e (cm^{-1})	$E_0=\frac{1}{2}h\nu_0$	D_e (cm^{-1})	$U_{(r)}$ (kcal mole^{-1})
HCO→H+CO	H—C	1·11	2800	4·0	33,300	$95\,(1-e^{-2\cdot02})^2$
	C—O	1·21	1700	2·4	65,000	$185\,(1-e^{-2\cdot58})^2$
$CH_3CO\rightarrow CH_3+CO$	C—C	1·55	1000	1·4	29,800	$85\,(1-e^{-2\cdot72})^2$
	C—O	1·22	1700	2·4	65,000	$185\,(1-e^{-2\cdot58})^2$
COCl→CO+Cl	C—Cl	1·74	850	1·2	26,300	$75\,(1-e^{-2\cdot26})^2$
	C—O	1·18	1800	2·6	70,000	$200\,(1-e^{-2\cdot72})^2$

The carbonyl parameters are not critical owing to the position of the crossing point, for example, if r_e C—O in HCO is 1·19 Å, then E_c will be decreased by ~1 kcal mole^{-1}.

The D_e values were chosen using 258 kcal mole^{-1} for the dissociation energy of carbon monoxide, which is consistent with a latent heat of vaporization of carbon of 170 kcal mole^{-1}. On the other hand, if this latter value is taken to be 136 kcal mole^{-1}, then the final activation energies will be 1–2 kcal mole^{-1} lower for CH_3CO and practically unchanged for HCO. The values for the carbonyl bonds in the radicals were estimated by taking 60–70 kcal mole^{-1} as the reorganization energy in COCl (Burns and Dainton 1952) and rounding off the

COCl D_e value to 200 kcal mole^{-1}. Thence for HCO and CH_3CO the corresponding carbonyl bond lengths of CH_3CHO and HCHO (about 1·21–1·22 Å) compared to $COCl_2$ (1·18 Å, Allen and Sutton 1950) gave a rounded off figure of 185 kcal mole^{-1} from bond length *v.* bond energy tables (Skinner 1945).

The surface I as prepared makes no allowance for interbond effects. The correction for interbond forces, at any point, may be estimated using the linear harmonic oscillator formula for the potential energy V, that is,

$$2V = f_1\Delta r_1^2 + f_2\Delta r_2^2 + 2f_{12}\Delta r_1\Delta r_2,$$

where the f's are the respective force constants. If f_{12} is known, the ratio of the interbond energy to the bond energy may be obtained at $\triangle r_1 \triangle r_2$ (Table 2) (see Duchesne and Burnelle 1949, 1951; Stearn and Eyring 1935; Coulson, Duchesne, and Manneback 1947).

TABLE 2

CORRECTIONS FOR INTERBOND EFFECTS AT THE CROSSING POINT

Linear Formula	f_1	f_2	f_{12}	Correction at Crossing Point (%)
HCO	5	13	−1	−3
CH_3CO	4	13	+1	+6
COCl	3	13	+1	+6

Although the f values are very approximate owing to the free electron of the radicals and the assumption of a linear structure, the correction to E_e can hardly be greater than $\frac{1}{2}$ kcal mole^{-1}.

III. The Collision Surface for R and CO (Surface II)

The collision surface was constructed using the relation

$$U_{(r)} = -cr^{-6} + br^{-9},$$

the first term giving the van der Waals attraction and the second term the repulsion between the colliding particles. The constant c is given by $\frac{3}{2}h(\alpha_1\alpha_2\nu_1\nu_2/\nu_1+\nu_2)$; α_1 and α_2 being the polarizabilities of the colliding particles and ν_1 and ν_2 their fundamental frequencies. The constant b is found in terms of c by the condition that

$$\left.\frac{\partial U}{\partial r}\right|_{r=r_0} = 0,$$

and the equation now becomes

$$U_{(r)} = \frac{c}{r^6}\left\{\frac{2}{3}\left(\frac{r_0}{r}\right)^3 - 1\right\},$$

where r_0 is the equilibrium interparticle distance, $\nu = I_e/h$, and $\alpha = r_0^3$; I_e being the ionization potential. The collision surface was constructed in an analogous

fashion to the vibrational surface. A family of repulsion curves was drawn, each curve corresponding to a particular C—O distance, and separated from its neighbour by the energy required to stretch or compress the C—O bond. The contours of the collision surface follow from this family of curves.

In constructing this surface the major difficulties occur in deciding the correct polarizability and radius of the colliding particles. In particular when the particles are very close the parameters used will be incorrect and a "resonance" correction will be required. This resonance correction was estimated to be about 7 kcal mole^{-1} from the COCl reaction. Sufficient accuracy should still be obtainable to decide the equality or otherwise of the formyl and acetyl energies of activation.

The theory of intermolecular forces between spherical non-polar particles to which H, CH_3, Cl, and CO reasonably approximate has been discussed by London (1937, 1942), Margenau (1938, 1939), Glasstone (1944), Beattie and Stockmayer (1951), Hornig and Hirschfelder (1952). The constants in the power series expansion starting with r^{-6} for like and unlike particle attraction have been given by Margenau and also by Hornig and Hirschfelder. Apart

TABLE 3

PARAMETERS USED IN COMPUTING REPULSION SURFACES

Reaction	Radical	I_e (eV)	α (cm^3 mole^{-1} $\times 10^{24}$)	r_0 (Å)	ΔH (kcal mole^{-1})
HCO→H+CO	H	13·6*	0·67	0·85	23±3
	CO	14·1*	2·0	1·25	
$CH_3CO \rightarrow CH_3+CO$	CH_3	10·0†	2·0	1·25	~16
COCl→CO+Cl	Cl	13·0‡	1·8	1·22	6§

* Herzberg (1950).
† Eltenton (1947).
‡ Gaydon (1953).
§ Burns and Dainton (1952).

from H/H collisions, the convergence is sufficiently rapid so that a one-term expression is sufficient, the difficulty with H/H arising from both particles having oscillator strength values less than unity. A check of the three-term expansion to r^{-10} using Margenau's formula involving the oscillator strengths showed that H_2/H_2, Cl_2/Cl_2, and Cl/Cl collisions gave higher va ues by 1–5 kcal mole^{-1} at the 30 kcal mole^{-1} value of $U_{(r)}$, compared with the one-term r^{-6} form. The rounded-off value of $r_0=3\sqrt{\alpha}$ (cf. Glasstone 1944) was used as a consistent parameter value.

The simple br^{-n} ($n=9$) expression was used for the repulsion energy instead of the exponential form ($be^{-r/\rho}$), since the latter contains two disposable parameters; the former appears to give good results. The parameters used are shown in Table 3. The ΔH is used to place surface II vertically relative to surface I; the values are estimated as set out below from thermochemical cycles and bond-energy data (Skinner 1945; Pitzer 1948). The probable

errors of several kcal mole^{-1} only affect the activation energies by $\sim$1 kcal mole^{-1} owing to the low angle of the crossing surfaces (see Fig. 2).

HCO: Dissociation energy = D.E. = 76 kcal mole^{-1}, and $\Delta H = 99 - 76 = 23$ kcal mole^{-1}.

$$\begin{array}{ccc} CH_3CHO & \xrightarrow{D.E.} & CH_3 + CHO \\ 4 \uparrow & & \downarrow \Delta H \\ CH_4 + CO & \xrightarrow[103]{} & CH_3 + H + CO \end{array}$$

CH_2CO: Dissociation energy = D.E. = 83 kcal mole^{-1}, and $\Delta H = 99 - 83 = 16$ kcal mole^{-1}.

$$\begin{array}{ccc} CH_3CHO & \xrightarrow{D.E.} & H + CH_2CO \\ 4 \uparrow & & \downarrow \Delta H \\ CH_4 + CO & \xrightarrow[103]{} & CH_3 + H + CO \end{array}$$

COCl: Dissociation energy = D.E. = 75 kcal mole^{-1}, and $\Delta H = 81 - 75 = 6$ kcal mole^{-1}.

$$\begin{array}{ccc} COCl_2 & \xrightarrow{D.E.} & Cl + COCl \\ -24 \uparrow & & \downarrow \Delta H \\ CO + Cl_2 & \xrightarrow[57]{} & CO + 2Cl \end{array}$$

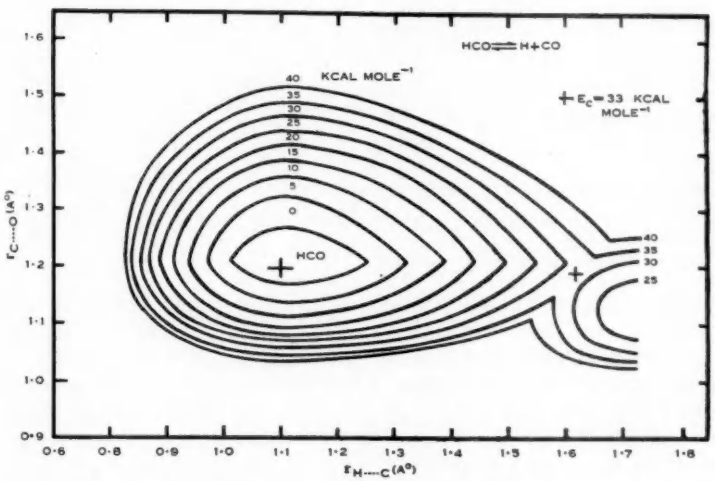

Fig. 1.—The potential energy surface for the reaction HCO⇌H+CO.

The polarizability of CO is given by Denbigh (1940, 1949) as $\alpha_l = 2 \cdot 6 \times 10^{-24}$ cm^3 mole^{-1} and $\alpha_t = 1 \cdot 6 \times 10^{-24}$ cm^3 mole^{-1}, so that a mean value of 2×10^{-24} cm^3 mole^{-1} should be reasonable. For Cl the value of $1 \cdot 8 \times 10^{-24}$ cm^3 mole^{-1} has been chosen by analogy with argon ($1 \cdot 6 \times 10$ cm^3 mole^{-1}), whilst for CH_3 the value of 2×10^{-24} cm^3 mole^{-1} is taken by calculating the

three CH polarizabilities as 1·7, together with the contribution from the free electron.

The zero for each surface was arbitrarily chosen at the position of the zero-point energy and the scale taken as positive upwards. The horizontal placement of the surfaces with respect to each other is effected by assuming r to be the continuation of the interatomic distance of the bond broken and this, though approximate, is feasible for comparative purposes.

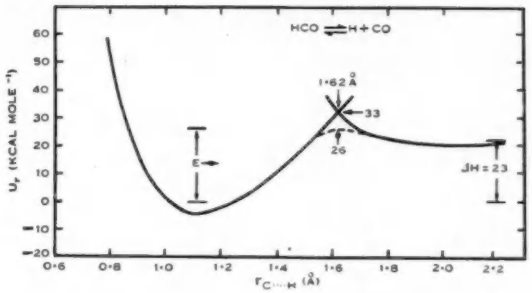

Fig. 2.—The reaction path showing the relation between E_c and the decomposition activation energy.

Figure 1 represents the energy surface for the decomposition of the HCO radical, whilst Figure 2 gives a section through the surface along the reaction path. The CH_3CO and COCl surfaces resemble Figure 1 closely and are therefore not reproduced. Table 4 summarizes the results from the calculations.

TABLE 4

ENERGIES OF ACTIVATION FOR DECOMPOSITION AND FORMATION OF RADICALS

Reaction	E_c*	Resonance Energy	$\overrightarrow{E}_{act.}$ (kcal mole^{-1})	ΔH	$\overleftarrow{E}_{act.}$ (kcal mole^{-1})
$HCO \rightleftharpoons H+CO$ ..	33	7	26	23	3
$CH_3CO \rightleftharpoons CH_3+CO$ ..	25	7	18	16	2
$COCl \rightleftharpoons CO+Cl$ ..	13	7	6	6	0

* E_c is the energy of the crossing point.

The conclusion is drawn that the formyl decomposition energy of activation is ~10 kcal mole^{-1} higher than that for acetyl.

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THE PHOTOLYSIS OF GASEOUS ALDEHYDES

III. FORMALDEHYDE AND MIXTURE OF FORMALDEHYDE WITH ACETALDEHYDE, ACETONE, AND CARBON DIOXIDE

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Summary

The mechanism of formaldehyde photolysis proposed by Calvert and Steacie (1951) has been re-examined and a formyl chain step included as an essential part of the reaction. In addition, formyl radical decomposition has been considered as a bimolecular process with a higher energy of activation than that assumed by Calvert and Steacie, a result in agreement with the conclusions of the preceding paper of the present series. The experimental energy of activation for the overall photolysis was found to vary continuously with temperature even at 300 °C, where it was 14 kcal mole^{-1}; this value cannot be assigned to a single stage in the reaction.

I. INTRODUCTION

The primary purpose of this investigation was to obtain additional information on the stability and reactions of the formyl radical, the behaviour of which is of some importance in the photolysis of acetaldehyde (Dorman and Buchanan 1956*a*, 1956*b*, Parts I and II of this series). In brief, the evidence indicates that HCO is stable at least up to 200 °C, and begins to decompose appreciably above this temperature. The resulting H atoms initiate chains of decomposition by their attack on CH_3CHO, which gives the unstable (at these temperatures) CH_3CO radical, thus ultimately producing chain-propagating methyl radicals.

The mixture experiments were confined to rate studies and yielded useful confirmatory evidence on the mode of decomposition of the formyl radical and on the relative stabilities of formyl and acetyl.

II. THE PHOTOLYSIS OF HCHO

This photolysis has been re-examined by Calvert and Steacie (1951), who propose the following mechanism:

$$\begin{aligned} HCHO &\xrightarrow{h\nu} H + HCO, \\ H + HCHO &\longrightarrow H_2 + HCO, \\ HCO &\longrightarrow H + CO, \\ HCO + Wall &\longrightarrow Product. \end{aligned}$$

Calvert and Steacie attributed the overall energy of activation (obtained from an apparently linear part of the log (rate) *v.* $1/T$ curve, above 200 °C) to the

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decomposition of the formyl radical. The resulting value of about 13 kcal mole^{-1} seemed somewhat low in the light of our acetaldehyde results. In addition, a theoretical study, using Bawn's (1938) method, of the comparative energies of activation for decomposition gave 6, 18, and 26 kcal mole^{-1} for the related COCl, CH_3CO, and HCO radicals respectively (Part II loc. cit.). The experimental evidence on CH_3CHO photolysis clearly indicated that formyl was more stable than acetyl (Part I).

As the analysis and the experimental results presented in this paper indicate, it is likely that the overall energy of activation value for HCHO photolysis is not to be attributed to one process (i.e. formyl decomposition) but is rather, a complex quantity. We have reconsidered the photolysis mechanism in detail, and the reactions shown in Table 1 are possible.

TABLE 1

POSSIBLE REACTIONS IN THE PHOTOLYSIS OF FORMALDEHYDE

Reaction	Rate	Step	Notation
$HCHO \xrightarrow{h\nu} H+HCO$	$\varphi I_{abs.}$	1	z
$HCO+M \longrightarrow H+CO+M$	k_2	2	k
$H+CO \longrightarrow HCO$	k_{2a}	2a*	a
$H+HCO \longrightarrow HCHO$	k_3	3*	d
$H+HCHO \longrightarrow H_2+HCO$	k_4	4	b
$H \xrightarrow{wall} \frac{1}{2}H_2$	k_5	5	c
$HCO+HCHO \longrightarrow H_2+CO+HCO$	k_6	6	e
$HCO+HCO \longrightarrow (HCO)_2$ or H_2+2CO ..	k_7	7	f
$HCO \xrightarrow{wall} \frac{1}{2}H_2+CO$	k_8	8	g
$HCO+H_2 \longrightarrow HCHO+H$	k_9	9	i

* Probably insignificant.

In the temperature range 120 to 350 °C it seems likely that Calvert and Steacie's (1951) mechanism is too simple in that it neglects the possibility of a formyl chain mechanism (reaction (**6**)), and also the pressure dependence of the formyl radical decomposition (reaction (**2**)) (cf. Benson 1952).

Considering the above mechanism, the steady state method yields the following relations :

$$\frac{d[H]}{dt}=0=\varphi I_{abs.}-k_{2a}[H][CO]+k_2[HCO][M]-k_3[H][HCO] -k_4[H][HCHO]-k_5[H]+k_9[HCO][H_2], \quad \ldots\ldots\ldots (1)$$

$$\frac{d[HCO]}{dt}=0=\varphi I_{abs.}+k_{2a}[H][CO]-k_2[HCO][M]-k_3[H][HCO] +k_4[H][HCHO]-2k_7[HCO]^2-k_8[HCO]-k_9[HCO][H_2], \quad \ldots\ldots\ldots\ldots\ldots (2)$$

$$\frac{d[CO]}{dt}=\alpha=-k_{2a}[H][CO]+k_2[HCO][M]+k_6[HCO][HCHO] +2k_7[HCO]^2+k_8[HCO], \quad \ldots\ldots\ldots\ldots\ldots (3)$$

$$\frac{d[H_2]}{dt}=\alpha=k_4[H][HCHO]+\tfrac{1}{2}k_5[H]+k_6[HCO][HCHO]$$
$$+k_7[HCO]^2+\tfrac{1}{2}k_8[HCO]-k_9[HCO][H_2], \quad \ldots\ldots\ldots\ldots \quad (4)$$

$$\frac{d[HCHO]}{dt}=-\alpha=-\varphi I_{abs.}+k_3[H][HCO]-k_4[H][HCHO]$$
$$-k_6[HCO][HCHO]+k_9[HCO][H_2]. \quad \ldots\ldots\ldots\ldots \quad (5)$$

Let

$a=k_{2a}[CO]$, $d=k_3$, $g=k_8$, $x=[H]$,
$b=k_4[HCHO]$, $e=k_6[HCHO]$, $k=k_2[M]^*$, $y=[HCO]$,
$c=k_5$, $f=k_7$, $i=k_9[H_2]$, $z=\varphi I_{abs.}$.

It will be noted that

equation (2)=equation (3)+equation (5),

and that

equation (1)=equation (2)+2{equation (3)-equation (4)}.

Equations (3), (4), and (5) now become:

$$-ax+ky+ey+2fy^2+gy=\alpha, \quad \ldots\ldots\ldots\ldots \quad (3)$$
$$bx+\tfrac{1}{2}cx+ey+fy^2+\tfrac{1}{2}gy-iy=\alpha, \quad \ldots\ldots\ldots\ldots \quad (4)$$
$$-z+dxy-bx-ey+iy=-\alpha. \quad \ldots\ldots\ldots\ldots \quad (5)$$

Neglecting terms involving the second power of radical concentrations, we obtain

$$-ax+y(k+e+g)=\alpha, \quad \ldots\ldots\ldots\ldots \quad (3)$$
$$x(b+\tfrac{1}{2}c)+y(e+\tfrac{1}{2}g-i)=\alpha, \quad \ldots\ldots\ldots\ldots \quad (4)$$
$$-z-bx-y(e-i)=-\alpha. \quad \ldots\ldots\ldots\ldots \quad (5)$$

From (3)

$$y=\frac{ax+\alpha}{k+e+g}, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

and substituting for y in (4) we obtain

$$(b+\tfrac{1}{2}c)x+\frac{(e+\frac{1}{2}g-i)(ax+\alpha)}{(k+e+g)}=\alpha,$$

therefore

$$x=\frac{\alpha(k+\frac{1}{2}g+i)}{a(e+\frac{1}{2}g-i)+(k+e+g)(b+\frac{1}{2}c)}, \quad \ldots\ldots\ldots \quad (7)$$

By taking $[H_2]=[CO]$, sufficiently small, we may eliminate the i and a terms, thus,

$$x=\frac{\alpha(k+\frac{1}{2}g)}{(k+e+g)(b+\frac{1}{2}c)}, \quad \ldots\ldots\ldots\ldots\ldots \quad (8)$$

$$y=\frac{\alpha}{k+e+g}, \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (9)$$

$$z=\alpha-bx-ey. \quad \ldots\ldots\ldots\ldots\ldots \quad (10)$$

* $[M]=[HCHO]$.

Substituting for x and y in (**10**) we obtain

$$z=\alpha-\frac{b\alpha(k+\frac{1}{2}g)}{(k+e+g)(b+\frac{1}{2}c)}-\frac{e\alpha}{k+e+g}.$$

If b is taken to be much greater than c, that is $k_4[\mathrm{HCHO}]\gg k_5$ (wall loss of H atoms insignificant), then

$$z=\alpha\left\{1-\frac{k+\frac{1}{2}g}{k+e+g}-\frac{e}{k+e+g}\right\}$$

$$=\frac{\alpha}{2}\cdot\frac{g}{k+e+g}. \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \textbf{(11)}$$

Equation (**11**) shows the proportionality of rate α to light intensity z at constant [HCHO] as found by Calvert and Steacie.

For two temperatures T_1 and T_2, $z(T_1)=z(T_2)$ (since $z=\varphi I_{\mathrm{abs.}}$), and hence

$$\frac{(k+e+g)_{T_1}}{(k+e+g)_{T_2}}=\frac{(\alpha g)_{T_1}}{(\alpha g)_{T_2}}. \quad \ldots\ldots\ldots\ldots\ldots\ldots \textbf{(12)}$$

If now we assume $k\gg e$, $g_{T_1}=g_{T_2}=g$ and $k\gg g$ (i.e. the rate of formyl decomposition in the presence of M is much greater than the rate of formyl reaction with HCHO, or the rate of formyl decomposition on the walls), then we obtain

$$\frac{k_{T_1}}{k_{T_2}}=\frac{\alpha_{T_1}}{\alpha_{T_2}}, \quad \ldots\ldots\ldots\ldots\ldots\ldots \textbf{(13)}$$

that is

$$\frac{e^{-E_2/RT_1}}{e^{-E_2/RT_2}}=\frac{\alpha_{T_1}}{\alpha_{T_2}},$$

and

$$e^{E_2/R\left(\frac{1}{T_1}-\frac{1}{T_2}\right)}=\frac{\alpha_{T_2}}{\alpha_{T_1}}. \quad \ldots\ldots\ldots\ldots\ldots\ldots \textbf{(14)}$$

Equation (**14**) is that given by Calvert and Steacie (1951) for the apparently linear part (190–300 °C) of their Figure 3, and leads to $E_2=13$ kcal mole^{-1}.

Using Calvert and Steacie's results, we may arrive at approximate values for the terms of equation (**11**):

$z_{T_1}=z_{T_2}=7\cdot6\times10^{11}$ quanta c.c.$^{-1}$ sec^{-1} (assuming $\varphi=1$),
$\alpha_{T_1}=4\cdot0\times10^{12}$ molecule c.c.$^{-1}$ sec^{-1} $T_1=468$ °K,
$\alpha_{T_2}=51\times10^{12}$ molecule c.c.$^{-1}$ sec^{-1} $T_2=568$ °K,
$[\mathrm{HCHO}]=5\cdot8\times10^{-6}$ mole c.c.$^{-1}$.

$$\left\{\frac{g}{k+e+g}\right\}_{T_1=468^\circ\mathrm{K}}=0\cdot4, \quad \ldots\ldots\ldots\ldots \textbf{(15a)}$$

$$\left\{\frac{g}{k+e+g}\right\}_{T_2=568^\circ\mathrm{K}}=0\cdot03. \quad \ldots\ldots\ldots\ldots \textbf{(15b)}$$

Values of k, e, and g to satisfy equations (**15a**) and (**15b**) may be found by trial as follows:

$g=g_1=g_2\simeq 0\cdot 2$ sec^{-1} (temperature independent loss of formyl radicals on the walls),

k (pressure dependent) $=10^{14}[\mathrm{HCHO}]e^{-E_2/2T}$,

k (pressure independent) $=10^{13}e^{-E_2/2T}$,

$e=10^{-5}.10^{14}[\mathrm{HCHO}]e^{-E_6/2T}$ (see Table 2; also Frost and Pearson 1953).

TABLE 2

ALTERNATIVE COMBINATIONS OF VALUES OF ENERGIES OF ACTIVATION FOR FORMYL RADICAL REACTIONS IN FORMALDEHYDE PHOTOLYSIS

Temp. (°K)	Nature of Formyl Decomposition	E_2 (kcal mole^{-1})	E_6 (kcal mole^{-1})	$\frac{g}{k+e+g}$
468	Pressure dependent ..	23*	10	0·54
568		23	10	0·06
468	Pressure independent ..	23	10	$3\cdot 18\times 10^{-4}$
568		23	10	$5\cdot 13\times 10^{-6}$
468	Pressure dependent ..	13	10	$4\cdot 14\times 10^{-4}$
568		13	10	$3\cdot 13\times 10^{-6}$
468	Pressure independent ..	13	10	$2\cdot 41\times 10^{-8}$
568		13	10	$1\cdot 82\times 10^{-9}$
468	Pressure dependent ..	13	5	$3\cdot 91\times 10^{-4}$
568		13	5	$3\cdot 09\times 10^{-5}$

* A weighted minimum value estimated from Part II (Dorman and Buchanan 1956*b*).

It is evident that the combination of $E_2=23$ kcal mole^{-1}, $E_6=10$ kcal mole^{-1}, and pressure dependent decomposition of the formyl radical is the only one of the above alternatives giving acceptable agreement with the experimental

TABLE 3

INFLUENCE OF CARBON DIOXIDE ON THE RATE OF FORMALDEHYDE PHOTOLYSIS

At temperature 305 °C

p-HCHO (cm Hg)	p-CO_2 (cm Hg)	Rate (cm water/min)
10·6	—	1·14
10·0	5·0	1·36
10·0	10·0	1·40
9·4	18·5	1·80

figures. However, this result is not unique in that an increase of several kcal mole^{-1} in E_6 makes the term e insignificant. It is also dependent on a low probability factor (10^{-5}) for formyl radical reaction with HCHO (reaction

(**6**)); this seems reasonable. In any case, provided that the frequency factor for reaction (**2**) is normal, a value of 13 kcal mole^{-1} for E_2 cannot be accepted.

The value of $g \simeq 0 \cdot 2$ sec^{-1} agrees with the probable order of magnitude of $0 \cdot 1$ obtained from theoretical equations and experimental results for H atom wall loss of Smith (1943).

On rearranging equation (**11**) and writing it out in full, we obtain

$$\alpha = \text{rate} = \frac{2\varphi I_{\text{abs.}}(k_2[\text{M}] + k_6[\text{HCHO}] + k_8)}{k_8}.$$

In view of this equation and of the above discussion, it is evident that the overall E value of 13 kcal mole^{-1} found by Calvert and Steacie cannot be referred to a single reaction.

As the temperature decreases, reaction (**7**) (formyl "recombination") should increase in importance, whilst the chain step (**6**) becomes unimportant, thus leaving reaction (**4**) (non-chain) and (**8**) (formyl loss on the walls) as the major processes. The experimental activation energy should accordingly diminish (see below).

Taking values of k, e, and g at 500 °K from the above figures, we find $[\text{H}] = 10^{-7}$ mole c.c.$^{-1}$, $[\text{HCO}] = 10^{-11}$ mole c.c.$^{-1}$, and hence to exclude reaction (**7**) (formyl recombination) we find

$$\frac{\text{rate of HCO wall decomposition}}{\text{rate of HCO recombination}} = \frac{0 \cdot 2}{A \times 10^{-11}}.$$

Hence $A \sim 10^{10}$ c.c. mole^{-1} sec^{-1} in order to eliminate significant formyl recombination at this temperature, assuming near zero activation energy for the radical recombination (as is generally the case), a probability factor of 10^{-3} would appear reasonable for combination of non-linear formyl radicals (Ramsay 1953).

III. Experimental Results

Formaldehyde was prepared from *p*-formaldehyde by the method of Spence and Wild and stored as a liquid at −80 °C. A Pyrex reaction vessel (length 16 cm, radius $1 \cdot 5$ cm, and volume 115 c.c.) with plane end windows (cutting off virtually all radiation below λ 3100 Å) was irradiated in a furnace with silica end windows. The light was obtained from a 125 W medium pressure mercury arc and was first passed through a 6 cm water cell. A HCHO pressure of 30 cm Hg at 300 °C was irradiated for periods of from 3 to 10 min and the mixture was then pumped into a −183 °C trap. The non-condensable gases at this temperature were then collected and measured. The connecting tubes of the apparatus were wire-wound and heated to about 85 °C, the taps being greased with "Apiezon T" grease. Some polymerization of HCHO occurred at the taps and pressure changes were allowed for where necessary. Calibration blank runs (no irradiation) permitted checking for tap leaks and HCHO elimination in the liquid oxygen traps.

The rate of the reaction was calculated from the volume of the residual gases at −183 °C (H_2+CO). A plot of log (rate) *v.* $1/T$ then gave a non-linear

curve over the temperature region 198–352 °C (Fig. 1). Calvert and Steacie (1951) obtain a straight line but their highest point indicates that non-linearity is quite probable. The experimental points in Figure 1 indicate the accuracy obtained.

Summarizing the experimental energies of activation, we obtain :

Temperature range (0 °C) :	198–307,	198–257,	257–307
E (kcal mole^{-1}) :	12·1	11·1	13·9

The overall value (198–307 °C) is in good agreement with that of Calvert and Steacie, but there is no doubt that E increases with temperature, as would be

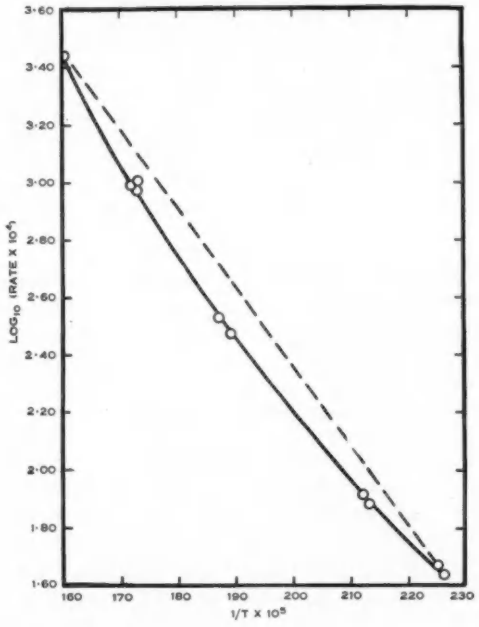

Fig. 1.—Activation energy plot for the high temperature photolysis of HCHO ($\lambda > 3100$).

expected from the above discussion. It is suggested that the closer approach to linearity of Calvert and Steacie's results, where the difference of " linearity " and " non-linearity " is of the same order of magnitude as the experimental error, is due to the low light intensity used. The more non-linear curve obtained in the present work probably involves a significant contribution by reaction (7) at temperatures above 200 °C ; the main point, however, is that, if there is non-linearity up to 300 °C, then Calvert and Steacie's mechanism is incomplete.

IV. Formaldehyde Photolysis in the Presence of CO_2

The photolysis rate was observed by following the pressure change with a Bourdon gauge, a silica reaction vessel and a medium pressure Hg arc being used.

An increase in rate was observed, although the effect was smaller than that reported by Calvert and Steacie (Table 3).

The effect is presumably due to an increase in the rate of reaction (**2**) (increase in [M]) and hence an increase in the rate of the chain step (**4**). The results of Calvert and Steacie indicate a collision efficiency of about 0·9 for CO_2 in the formyl decomposition reaction, whilst the results of Table 3 correspond to a value of about 0·7. However, the difference may have been connected with a higher light intensity in the present experiments.

V. Formaldehyde Photolysis in the Presence of CH_3CHO and CH_3COCH_3

The rates with these mixtures were observed as above. The addition of HCHO to CH_3CHO at 300 °C markedly reduced the rate of photolysis of the latter (see Dorman and Buchanan 1956*c*, Part IV of this series). This effect may be due to the reaction

$$CH_3 + HCHO \rightarrow CH_4 + HCO,$$

the HCO being sufficiently stable, compared with CH_3CO, at this temperature to reduce the chain length of the CH_3CHO photolysis to some extent.

A mixture of 10 cm Hg of HCHO and 2·5 cm Hg CH_3COCH_3 gave a 30 per cent. increase over the HCHO rate at 305 °C, the CH_3COCH_3 rate alone being almost negligible. This result could be due to the above reaction (i.e. addition of methyl), the resultant formyl radical then decomposing by reaction (**2**) and ultimately causing chain decomposition of HCHO.

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THE PHOTOLYSIS OF GASEOUS ALDEHYDES

IV. MIXTURES OF ACETALDEHYDE WITH FORMALDEHYDE AND ACETONE, AND THE PHOTOLYSIS OF GLYOXAL

By F. H. DORMAN* and A. S. BUCHANAN*

[*Manuscript received October* 3, 1955]

Summary

The rate of acetaldehyde photolysis in presence of acetone showed an increase due to chain initiation by methyl radicals from the photo-decomposition of the acetone. In the presence of formaldehyde the acetaldehyde rate decreased, implying that the decomposition of formyl radicals was slower than that of acetyl. Glyoxal photolysis at long wavelengths confirmed previously found low ratios of H_2 to CO. Added acetaldehyde and formaldehyde decreased the rate of the photolysis possibly owing to collisional deactivation of excited glyoxal molecules.

I. INTRODUCTION

The mixture experiments were undertaken in an attempt to gain further evidence on the parts played by methyl and formyl radicals and by hydrogen atoms in he high temperature chain photolysis of acetaldehyde (see Dorman and Buchanan 1956*a*, Part I of this series).

II. EXPERIMENTAL

The reaction vessel and the arc were as described in Part I of this series. A Bourdon gauge and optical lever with a reading accuracy, under the operating conditions, of about 0·8 mm H_2O was used to measure the change in pressure. The change at the end of 1 min was recorded in cm H_2O. The reactant gases were mixed for 30 min in a separate container before admission to the reaction vessel; the walls of the latter were "cleaned" by several prior runs with acetaldehyde (irradiated) until a constant rate was observed. Formaldehyde was prepared and used as described in Part III of this series (Dorman and Buchanan 1956*b*). Acetone was purified by Shipsey and Werner's sodium iodide recrystallization after an initial permanganate treatment and distillation.

III. RESULTS

The graphs show the increase in rate in cm H_2O/min beyond the additive rates for the separate partial pressures in the mixtures of CH_3CHO and $(CH_3)_2CO$ (Fig. 1). The actual rate is compared with the additive rate for CH_3CHO and HCHO in Figure 2. With CO_2+CH_3CHO a 10 per cent. increase in the 1 min rates occurred for 10 cm Hg of CH_3CHO and 15 cm Hg CO_2 at 305 °C.

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IV. Discussion

Figure 1 shows that for small amounts of added methyl radical (from $(CH_3)_2CO$) a linear increase in rate occurs. For larger percentages of acetone

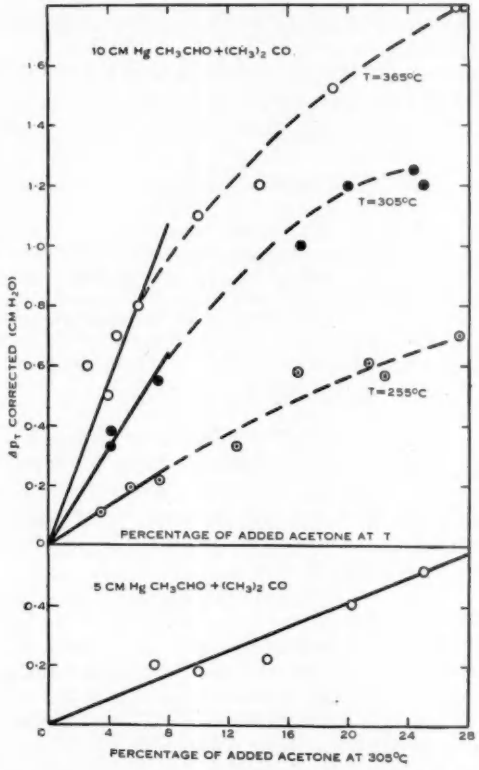

Fig. 1.—The increase in the initial rate over the separate rates for the high temperature photolysis of mixtures of $CH_3CHO+(CH_3)_2CO$.

non-linearity develops probably due to the reaction

$$CH_3\cdot+(CH_3)_2CO\rightarrow CH_4+CH_2COCH_3,$$

which breaks the methyl radical chains (as in the photolysis of acetone alone). Akeroyd and Norrish (1936) did not find any increase in rate of CH_3CHO photolysis in mixture experiments with acetone. However, these authors used a sufficient pressure of acetaldehyde to completely absorb the incident light, whilst our absorption was about 65 per cent. Grahame and Rollefson (1940), on

the other hand, found an increase for equal amounts of added acetone at 300 °C and λ 2650.

On comparing the increase in rate for 5 per cent. added acetone with 5 per cent. of the acetaldehyde rate, we find approximate equality in the temperature

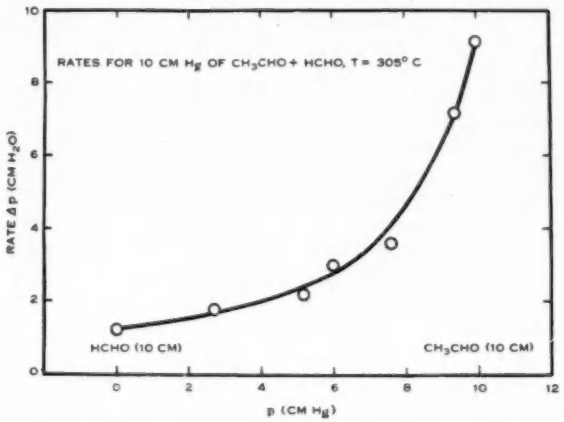

Fig. 2.—The initial rate of reaction for the photolysis of $HCHO+CH_3CHO$ at 305 °C.

region 250–350 °C (Table 1). Our experiments on iodine trapping of methyl radicals produced in acetone and acetaldehyde under the same conditions give double the rate of methyl radical production in the former as compared to the latter (Fig. 3).

TABLE 1

INCREASE IN THE RATE OF ACETALDEHYDE PHOTOLYSIS IN THE PRESENCE OF 5 PER CENT. OF ACETONE

Temp. (°C)	Rate CH_3CHO	Rate CH_3CHO (5%)	Increase for Added Acetone (5%)*
250	4	0·2	0·2
305	7	0·4	0·4
365	11	0·6	0·7

* Accuracy not high owing to drawing of gradients.

In Part I of this series Dorman and Buchanan (1956*a*) indicated that, in the case of CH_3CHO, the iodine trapping experiments measured only the *methyl* radicals produced initially, and hence the approximate equality shown in columns 3 and 4 of Table 1 can only be due to chains started by another radical in the CH_3CHO photolysis alone. This effect has already been discussed

in Part I as being due to H atom initiated chains above a temperature of ~ 250 °C (reactions (**4**, **5**, **3**, **2**)), the H atoms being produced by the decomposition of formyl radicals. We, therefore, now have further evidence for these reactions in the acetaldehyde photolysis.

The drop in rate of CH_3CHO photolysis in the presence of small amounts of added formaldehyde (Fig. 2) can be explained by the step

$$CH_3+HCHO \rightarrow CH_4+HCO.$$

Hence some of the acetyl radicals from reaction (**2**) (Part I) are now replaced by formyl radicals with a lower rate of decomposition. Since the rate of acetaldehyde chain photolysis is given approximately by $k[CH_3][CH_3CHO]$, it follows that, for a given temperature, the rate of photolysis will be reduced by the smaller methyl radical concentration.

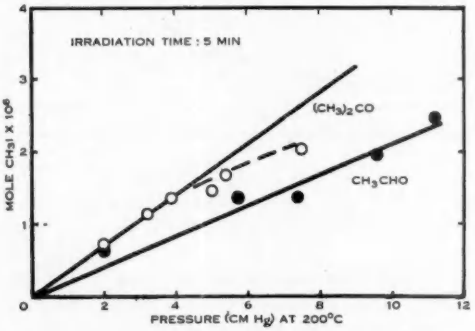

Fig. 3.—The formation of CH_3I in the irradiation of iodine-containing CH_3CHO and $(CH_3)_2CO$.

V. Photolysis of Glyoxal

(*a*) *Experimental*

The glyoxal was prepared by redistilling the product formed by heating the anhydrous polymer with P_2O_5. The reaction vessel was of Pyrex glass and the transmission below λ 3100 Å was negligible. Hence, using the medium pressure Hg arc, the principal lines available for the photolysis were λ 4360, 4050, and 3660 Å. The rate was observed by measuring the gases non-condensable at −183 °C. In certain cases this gas was analysed mass-spectrometrically for the ratio H_2/CO.

(*b*) *Results and Discussion*

For an irradiation time of 5 min at 182 °C, the rate *v.* pressure (over the range 3–9 cm Hg) gave a straighter curve than that of Calvert and Layne (1953). The overall activation energies, for pressures of about 13 cm Hg at 305 °C, were found to be 0·5 kcal mole^{-1} at 180 °C, 1·5 kcal mole^{-1} at 230 °C, and 2·5 kcal mole^{-1} at 260 °C, possibly indicating the beginning of a chain reaction.

The ratios H_2/CO were found to be 0·01 at 160 °C and 0·02 at 250 °C, which are considerably smaller than those of Calvert and Layne (1953) and may indicate a greater predominance of their reaction (**9**)

$$(HCO)_2^*\dagger \rightarrow H_2 + 2CO$$

over reaction (**2**),

$$(HCO)_2^* \rightarrow HCHO + CO.$$

It appears possible that the H atoms may be partially mobile along the O.C.C.O. conjugated system in the glyoxal molecule (however, cf. Coulson 1946), and on breaking the C—C or C—H bonds the H atom from one end of the molecule may migrate to the formyl radical fragment to give HCHO and CO as major products, with very little H_2. In the analogous case of biacetyl photolysis steric effects will probably prevent a similar migration of the CH_3 radical.

The addition of formaldehyde or acetaldehyde (but not CO_2) was found to lower the rate of the glyoxal photolysis. For a mixture of 8 cm Hg of glyoxal and 4 cm Hg of acetaldehyde at 198 °C (~60% light absorption by the former), the rate dropped by 22 per cent. of that for the 8 cm Hg of glyoxal, the acetaldehyde having a rate of only 16 per cent. that of the glyoxal. For the same pressure of glyoxal and 4·5 cm Hg of formaldehyde at 162 °C the drop in rate was 28 per cent., the formaldehyde alone having a rate only 2 per cent. of that of the glyoxal. Runs with both mixtures at 1 cm higher pressure of glyoxal confirmed these results and acted as a check for the incomplete absorption of the incident light by the glyoxal.

These results are difficult to explain unless deactivation of glyoxal without decomposition is assumed to occur. If this is the case, then formaldehyde, acetaldehyde, and presumably also glyoxal (as suggested by previous investigators) act as deactivators of the excited state. However, CO_2 does not appear to be effective in this respect, although Blacet and Moulton's (1941) results at room temperature indicate that both CO_2 and acetaldehyde increase the production of hydrogen.

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† $(HCO)_2^*$ represents an excited molecule.

THE EFFECT OF PRESSURE ON COMPLEX ION EQUILIBRIA

By A. H. Ewald* and S. D. Hamann*

[*Manuscript received September* 16, 1955]

Summary

The effect of pressure on the formation of complex ions in solutions of cobaltous chloride and in solutions containing iodine and iodide has been shown to be in qualitative agreement with a theory (Buchanan and Hamann 1953) attributing these effects primarily to changes in the free energy of solvation of the ions. The dissociation constant of tri-iodide ions in water at 22 °C has been shown to decrease from $1{\cdot}6\times10^{-3}$ mol kg^{-1} at atmospheric pressure to $1{\cdot}2\times10^{-3}$ mol kg^{-1} at 1500 atm. The enthalpy of dissociation of the tri-iodide ion was found to be approximately -5 kcal mol^{-1} and to be little affected by a pressure of 1500 atm.

I. Introduction

The effect of pressure on ionic equilibria has been the subject of several investigations in this laboratory (Buchanan and Hamann 1953; Hamann and Strauss 1955) and has been shown to be largely due to changes in the free energy of solvation of the ions. A very direct measure of this effect can be obtained by following colour changes induced by pressure in systems in which the participating ions absorb at characteristic wavelengths. This method has been used to investigate the formation of complex ions in a solution of cobaltous chloride in aqueous *iso*propyl alcohol and the formation of tri-iodide ions in a solution of iodine in aqueous potassium iodide. In the first of these systems the formation of the complex is accompanied by a decrease in the number of ionic charges, while this remains unchanged in the case of the iodine complex.

II. Cobaltous Chloride Solutions

Dilute aqueous solutions of cobaltous chloride are pink whereas concentrated aqueous solutions and solutions in organic solvents are blue. The nature of the ionic species causing the different colours has been widely discussed. The blue colour has been shown to be due to a complex anion and Sidgwick (1950) favours the theory of Donnan and Bassett that the equilibrium in a solution of cobaltous chloride is as shown in (1)

$$\underset{\text{pink}}{2Co^{++}}+4Cl^{-}\rightleftharpoons\underset{\text{blue}}{CoCl_4^{=}}+Co^{++}. \qquad \text{..... (1)}$$

The absorption of the blue ion has been found to be many times stronger than that of the pink ion and the presence of very little of the blue complex ion can completely mask the pink colour of the solution. All the ions must be considered

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to be solvated and it is possible that they will be present as ion pairs in solvents of low dielectric constant. Some qualitative observations of the effect of pressure on the absorption spectrum of aqueous cobaltous chloride solutions have previously been reported by Wick (1923).

(*a*) *Measurements*

The optical densities of the solutions were observed on a Unicam S.P.500 spectrophotometer which was adapted to be used with a special high pressure absorption cell. This stainless steel cell* has windows constructed on the principle described by Poulter (1932) and has been used at pressures up to 1500 atm. The solutions were contained in cylindrical Pyrex tubes which were closed by " Neoprene " plugs and were immersed in the transparent paraffin oil which filled the steel cell and served as the pressure transmitting medium.

Solutions of cobaltous chloride in dry *iso*propyl alcohol were found to be deep blue and to obey Beer's law over a range of 36-fold dilution. This shows that the salt was present entirely in the blue form. The molecular absorption coefficient of cobaltous chloride in this solvent was found to be independent of pressure and is shown as a full line in Figure 1. When *iso*propyl alcohol containing 2·91 per cent. (by volume) of water was used as solvent it was found that the solutions were of a much paler blue and that Beer's law no longer applied to them. The points in Figure 1 show the specific absorption S of these solutions at various concentrations. ($S=D/cl$, D=optical density, c=molar concentration of $CoCl_2$, l=length of absorption cell.)

The effect of pressure on one of the solutions in aqueous *iso*propyl alcohol (0·00604 mol kg^{-1} $CoCl_2$) is shown in Figure 2. The specific absorptions have been corrected for the increase in volume concentration due to the compression of the solution.†

The enthalpy of dissociation of the complex ion at atmospheric pressure was found to be $-4\cdot6$ kcal mol^{-1} from the change of optical density of one of the solutions between 70 °C and room temperature.

(*b*) *Discussion*

The effect of pressure on the solutions in aqueous *iso*propyl alcohol can be understood in terms of the change in the free energy of solvation accompanying the formation of the complex ion (Buchanan and Hamann 1953). Since this formation involves a decrease in the number of ionic charges there will be a decrease in the magnitude of the free energy of solvation. Pressure can be shown to favour an increase in the magnitude of the free energy of solvation and one would therefore expect the complex formation to be suppressed by pressure. Qualitatively this theory is therefore in agreement with the experimental results shown in Figure 2 which indicate that the concentration of the blue

* The authors wish to thank Mr. H. G. David of this laboratory for designing the high pressure equipment.

† The compressibility of aqueous *iso*propyl alcohol was measured in this laboratory by Mr. J. E. Stutchbury. At 1500 atm the correction amounted to 9 per cent.

complex decreases with pressure.* Unfortunately a quantitative test of the theory is not possible in this case since no equilibrium constant based on the simple equilibrium (1) could be found to fit the results. It is suggested that ion pair formation is superimposed on the equilibrium described by (1).

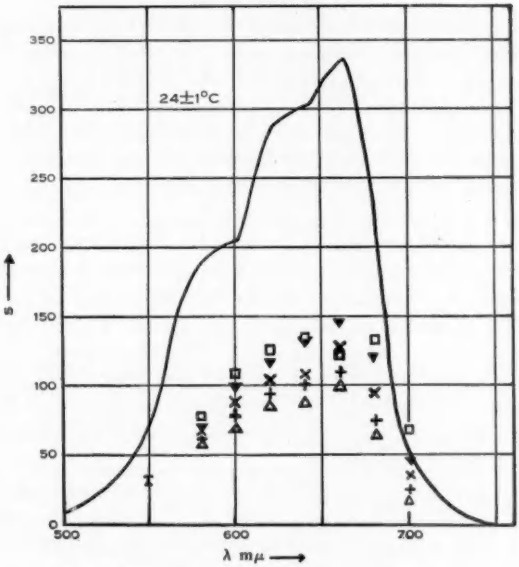

Fig. 1.—Absorption spectrum of $CoCl_2$ solutions.

Curve: molecular absorption coefficient of $CoCl_2$ in dry *i*-PrOH. The points denote specific absorption of solutions in *i*-PrOH + 2·91 per cent. H_2O. □ $62{\cdot}24\times10^{-3}$ mol kg^{-1} $CoCl_2$; ▼ $35{\cdot}50\times10^{-3}$ mol kg^{-1} $CoCl_2$; × $18{\cdot}15\times10^{-3}$ mol kg^{-1} $CoCl_2$; + $9{\cdot}075\times10^{-3}$ mol kg^{-1} $CoCl_2$; △ $3{\cdot}029\times10^{-3}$ mol kg^{-1} $CoCl_2$. Temperature 24 ± 1 °C.

III. Iodine Solutions

The effect of pressure on the formation of tri-iodide ions in aqueous solutions containing both iodine and iodide is of interest not only in itself, but also in connexion with the study of the rates of reactions involving iodine.

* *Note added in Proof.*—Since this paper was submitted for publication we have observed that a 0·05 mol kg^{-1} solution of copper sulphate in 2·5 mol kg^{-1} aqueous hydrochloric acid shows colour changes with temperature and pressure similar to those of cobalt chloride solutions. At atmospheric pressure such a solution is blue-green at room temperature but becomes yellow on heating. On compressing to 1600 atm the absorption at 400 mμ decreases to about half of its value at 1 atm. It is suggested that this absorption in the blue region of the spectrum is due to the complex $CuCl_4^{--}$ ion which is in equilibrium with Cu^{++} and Cl^- ions. As in the case of the cobalt solutions the concentration of the complex ion is decreased by pressure.

Ham (1954) studied the effect of pressure on the complexes formed between iodine and some benzene homologues and found it to be not very large. The effect of temperature on the equilibrium (**2**)

$$I_3^- \rightleftharpoons I_2 + I^-, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

in water-*tert.*-butyl alcohol was recently studied by Katzin and Gebert (1954) who rather surprisingly found the dissociation constant to decrease with a rise in temperature.

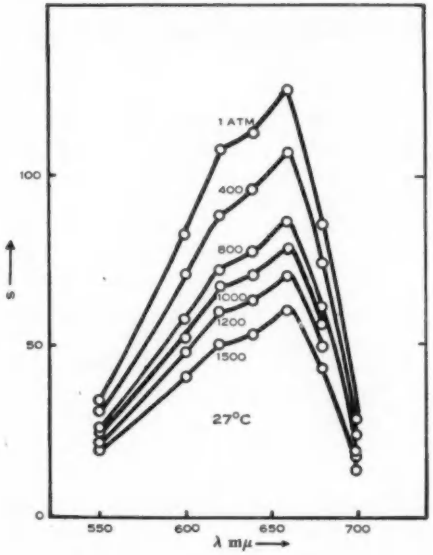

Fig. 2.—Effect of pressure on absorption spectrum of $CoCl_2$ solution at 27 °C $6{\cdot}04 \times 10^{-3}$ mol kg^{-1} $CoCl_2$ in *i*-PrOH+2·91% H_2O.

(*a*) *Measurements*

The apparatus used to investigate the iodine solutions was the same as that already described, except that a " Teflon " plug was used in the tube containing the iodine solution. The spectrum of the tri-iodide ions shows an absorption peak at 355 mμ, a wavelength at which neither iodine molecules nor iodide ions absorb appreciably, and it is therefore possible to measure the concentration of I_3^- spectrophotometrically (Awtrey and Connick 1951). The molecular absorption coefficient of I_3^- was determined in solutions containing a very large excess (10,000-fold) of iodide ions. These solutions were shown to obey Beer's law with reference to the iodine concentration, indicating that all the iodine was present as complex ions. The molecular absorption coefficient of the

tri-iodide ion was found to be $2{\cdot}81\times10^{4}$ mol^{-1} l. cm^{-1} at 355 mμ and was found to be independent of temperature and pressure within the range and accuracy of the measurements.

Equilibria were measured in solutions containing between $0{\cdot}893\times10^{-4}$ and $2{\cdot}443\times10^{-4}$ mol kg^{-1} of iodine and between two and four times as much potassium iodide. The dissociation constants which were found at various pressures and have not been corrected for activity are shown in Figure 3. The results of measurements at various temperatures at 1 and at 1500 atm are shown in Figure 4.

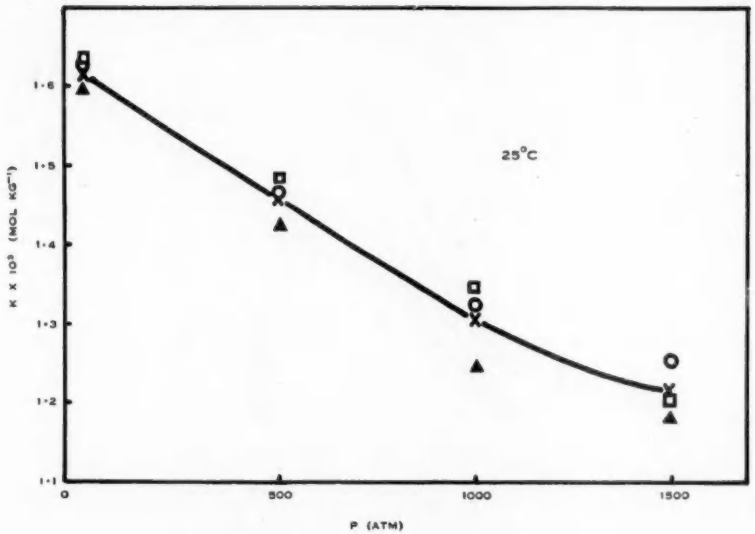

Fig. 3.—Effect of pressure on dissociation constant

$$K=\frac{[I_2][I^-]}{[I_3^-]}\ \text{mol kg}^{-1}\ \text{at 25 °C.}$$

The points denote the following molal concentrations: □ $1{\cdot}218\times10^{-4}$ I_2($4{\cdot}816\times10^{-4}$ KI); ○ $2{\cdot}443\times10^{-4}$ ($4{\cdot}842\times10^{-4}$); ▲ $1{\cdot}218\times10^{-4}$ ($2{\cdot}414\times10^{-4}$); × mean values.

(*b*) *Discussion*

The results shown in Figure 4 indicate that the dissociation constant of the tri-iodide ion increases with temperature contrary to the findings of Katzin and Gebert. The slopes of the two curves show that the enthalpy of dissociation is approximately −5 kcal mol^{-1} and is little affected by a pressure of 1500 atmospheres.

The effect of pressure on the dissociation constant of the tri-iodide ion is small, amounting to a decrease of about 20 per cent. at 1000 atm. The change

in partial molar volume accompanying the dissociation can be estimated from the slope of a plot of the logarithm of the dissociation constant against pressure and is found to be $+5{\cdot}4\ \mathrm{cm^3\,mol^{-1}}$. It is interesting to compare this value with the volume change calculated on the basis of simple models of the ions involved in the dissociation. Using crystallographic data for the distances between iodine atoms in the iodine molecule (2·66Å) and the tri-iodide ion (2·95Å), and using ionic and van der Waals radii for the size of the ions (2·16Å) and atoms (1·77Å), one finds a volume change of $+4{\cdot}92\ \mathrm{cm^3\,mol^{-1}}$ for the dissociation.

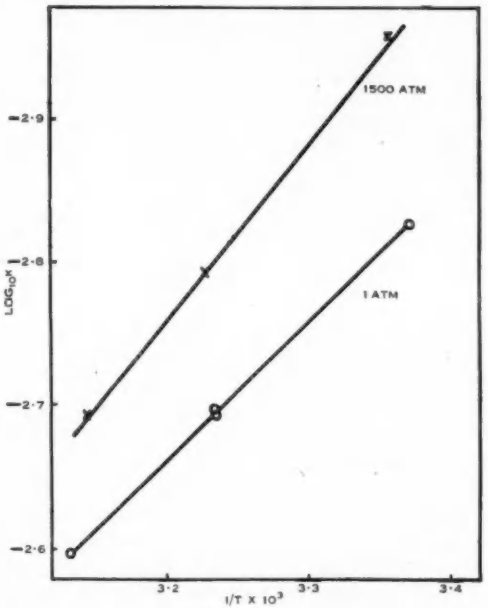

Fig. 4.—Effect of temperature on dissociation of tri-iodide ion.

It is thus apparent that most of the effect of pressure on the dissociation can be attributed to the change in the volume of the reacting species. The energy of solvation can therefore be only little affected by pressure, as would indeed be expected theoretically, since there is no change in the number of ionic charges in the dissociation.

IV. Acknowledgments

The authors are indebted to Prof. T. G. Hunter for providing accommodation and facilities in the Chemical Engineering Department of the University of Sydney.

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ELECTROPHILIC AND NUCLEOPHILIC SUBSTITUTION IN THE BENZENE RING AND THE HAMMETT EQUATION

By J. MILLER*

[*Manuscript received July* 1, 1955]

Summary

The Hammett equation as applied to aromatic nuclear electrophilic and nucleophilic substitution is tested for a wide range of substituents. For nucleophilic substitution quite good agreement is obtained for electron-attracting substituents using σ^* values, but large deviations occur with substituents releasing electrons by the conjugative mechanism. In electrophilic substitution, in so far as results are available, a fair measure of agreement obtains for electron-attracting substituents, but very large and to some extent irregular deviations occur for the conjugative electron-releasing substituents. The deviations occur whether σ or σ^* values are used, and new sets of σ_N^{**} and σ_E^{**} values are defined and the values recorded.

A comparison is made of substituent effects in nuclear electrophilic and nucleophilic substitution.

I. INTRODUCTION

A number of the previous publications of the author and co-workers (Miller 1951, 1952; Bolto and Miller 1953; Downing, Heppolette, and Miller 1953; Heppolette and Miller 1953, 1954; Heppolette, Miller, and Parker 1954; Miller 1954; Bolto, Liveris, and Miller 1955; Heppoette, Miller, and Williams 1955; Miller 1955) concerned with aromatic S_N reactions have dealt with the effects of *para*-substituents, and these have been represented by a substituent rate factor or S.R.F. (Miller 1952), equivalent to defining $\rho=1$ and using antilog σ in the Hammett equation (Hammett 1937, 1938). It is felt that there is much value in seeing how aromatic S_N reactions fit the Hammett equation, both for general interest, and for comparisons with aromatic S_E reactions in particular.

Jaffé (1953) has recently reviewed the basis and use of the Hammett equation, and quotes seven series of aromatic nuclear substitutions as fitting the equation. Of these, four are nucleophilic substitutions (Bunnett and Levitt 1948; Berliner and Monack 1952; Bevan 1953; Bunnett *et al.* 1953); two electrophilic (Ingold *et al.* 1931; Bird and Ingold 1938; Ingold and Smith 1938; Kuivila and Hendrickson 1952); and one free radical (Augood, Hey, and Williams 1952, 1953). The ρ value for the latter is only 0·675, but for the others the ρ values vary from 3·94 to 5·93 (ignoring sign).

A tendency for electron-releasing substituents to deviate from the equation is indicated by Jaffé (1953), and deviations are mentioned by some of the authors quoted above. Pearson, Baxter, and Martin (1952) have discussed the necessity

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for new more negative σ values for electron-releasing substituents in electrophilic substitution, and similar difficulties with these substituents are indicated by Bordwell* (1953, personal communication to Jaffé) and Hünig, Lehmann, and Grimmer (1953). With regard to nuclear electrophilic substitution, de la Mare (1954) has demonstrated a major lack of agreement for mainly electron-releasing substituents using particularly the results of de la Mare and Vernon (1951), and Robertson, de la Mare, and Swedlund (1953).

Jaffé (1953) has discussed the necessity for a special value of σ nominated σ* for reactions, particularly of amines and phenols, involving the conjugative (*T*) effects (Ingold 1953, p. 62) of *para*-substituents ; while Berliner and Monack (1952) have discussed the possibility that a further set of values, which will now be called σ** if referring to electron-releasing conjugative substituents, might be necessary for aromatic nuclear substitutions.

The results presented here for aromatic nuclear S_N reactions show that electron-attracting groups give a fairly adequate fit to the Hammett equation, using σ or σ* values as appropriate, while electron-releasing conjugative substituents do not. For aromatic nuclear S_E reactions fair agreement obtains for electron-attracting *meta*-substituents, while there are very large deviations for electron-releasing conjugative substituents in the *para*-position, as indicated by de la Mare (1954). From the Hammett plots (Figs. 2, 3, and 4) values of σ** are obtained, but the author prefers the use in general of the more flexible approach of Ingold (1953 ; cf. de la Mare 1954), with additional reference to the Hammett equation when, as here, useful information is obtainable from the appropriate σ values.

II. Experimental Data

Numerical Tables and Graphs

Table 1

substituted fluorobenzenes with OMe^- in MeOH at 0 °C†

Substituent	$\log_{10} k$	σ* Values	σ Values
H	−15·996	0	0
m-NO_2	−10·355	—	0·710
p-NO_2	− 5·203	1·270	—
p-N_2^+‡	0·230	(1·870)	—

† Owing to short range of temperature for measurements with the diazonium compound, and thus large probable error in activation energy, it was felt desirable to quote this compound only at an experimental temperature.

‡ After correction from original measurements with OH^- in H_2O using the experimental comparison OMe^- in MeOH to OH^- in H_2O for 4-bromo-3-nitrotrimethylanilinium chloride (Bolto, Liveris, and Miller 1955). Also includes experimental correction for ionic strength effects (Bolto and Miller, unpublished data).

* Quoted by Jaffé (1953).

TABLE 2

4-SUBSTITUTED 1-CHLORO-2-NITROBENZENES WITH OMe^- IN MeOH AT 50 °C

Values of σ^* in parentheses obtained from the ρ value determined from the other values plotted against $\log_{10} k$ to obtain it (Fig. 2).

Substituent	$\log_{10} k$	σ^* Values	σ Values
H	−5·599	0	0
F	−5·648	−0·015	—
Cl	−4·455	0·265	—
Br	−4·412	0·289	—
I	−4·358	(0·318)	0·276
CO_2^-†	−5·071	(0·135)	0·130
$CONH_2$	−3·182	0·627	—
CO_2Me	−2·406	0·636	—
		(0·819)	
COMe	−2·301	0·874	—
COPh	−2·175	(0·879)	—
NO_2	−0·541	1·270	—
$CH{=}CH{-}CO_2^-$† ..	−4·669	(0·239)	—
CH_3	−6·524	(−0·237)¶	−0·170
CF_3	−2·688	0·74	—
SO_3^-†‡	−4·876	0·381	—
		(0·186)	
SO_2NMe_2	−1·721	(0·995)	—
SO_2Me	−1·492	1·049	—
SO_2Ph§	−1·244	(1·117)	—
$N{=}N{-}Ph$|| ..	−2·981	(0·672)	0·640

† Includes correction for ionic strength effects (Bolto and Miller, unpublished data).

‡ Corrected from original measurements with OH^- in H_2O using the experimental comparison OMe^- in MeOH to OH^- in H_2O made for sodium 4-chloro-3,5-dinitrobenzoate (Briner and Miller 1954).

§ Corrected to value in MeOH from original measurements in 1 : 1 benzene-methanol using the comparison made experimentally with the corresponding COPh compound (Heppolette and Miller, unpublished data).

|| Miller and Parker, not previously recorded.

¶ More strictly a σ^{**} value.

TABLE 3

4-SUBSTITUTED 1-CHLORO-2,6-DINITROBENZENES WITH OMe^- IN MeOH AT 0 °C

Values of σ* in parentheses as for Table 2, but using ρ from Figure 3

Substituent	$\log_{10} k$	σ** Values (calc.)	σ* Values	σ Values
H	−4·303	0	0	0
Cl	−3·373	—	0·265	—
Br†	−3·246	—	0·289	—
CO_2^-‡	−3·693	—	(0·160)	0·132
$CONH_2$	−1·924	—	0·627	—
$CONMe_2$† ..	−2·492	—	(0·477)	—
CO_2Me	−1·442	—	0·636	—
			(0·753)	
COPh	−1·390	—	(0·767)	—
CH_3	−5·276	−0·256	—	−0·170
OMe	−6·567	−0·596	—	−0·260
NH_2	−7·588	−0·865	—	−0·660
C_6H_5§	−4·207	—	(0·025)	0·009
SO_3^-‡‖	−3·028	—	0·381	—
			(0·336)	

† Heppolette and Miller, not previously recorded.
‡ As footnote † of Table 2.
§ Bolto and Miller, not previously recorded.
‖ As footnote ‡ of Table 2.

TABLE 4

SUBSTITUTED BENZENES WITH Br_2 OR Cl_2 IN ACETIC ACID AT 25 °C

Substituent	$\log_{10}$ P.R.F.	σ** Values (calc.)	σ* Values	σ Values
H	0	0	0	0
p-NMe_2	19·5	−2·211	—	−0·600
p-OH	11·8	−1·338	—	−0·357
p-OMe	9·8	−1·111	—	−0·268
m-OMe	0·23	—	—	0·115
p-OPh	7·9	−0·896	—	−0·028
p-NHAc	9·1	−1·032	—	−0·015
p-CH_3	3·3	−0·374	—	−0·170
p-CMe_2	2·8	−0·318	—	−0·197
p-Ph	3·4	−0·386	—	0·009
p-F	0·8	−0·091	−0·015	—
p-Cl	−0·4	0·045	0·265	—
p-Br	−0·6	0·068	0·289	—
m-CO_2Et	−3·60	—	—	0·398
m-CO_2H	−3·89	—	—	0·315
m-NO_2	−6·05	—	—	0·710

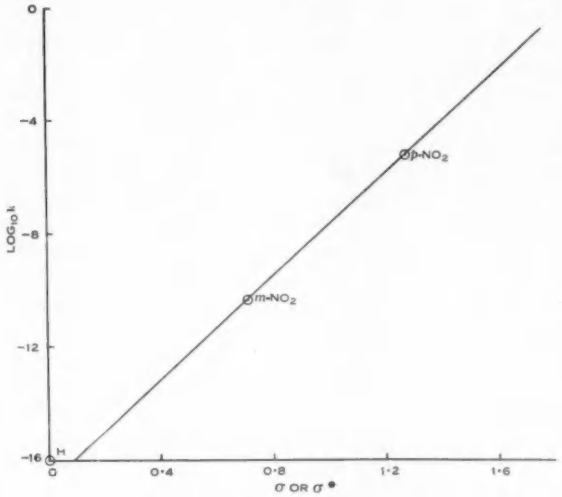

Fig. 1.—Fluorobenzenes at 0 °C.

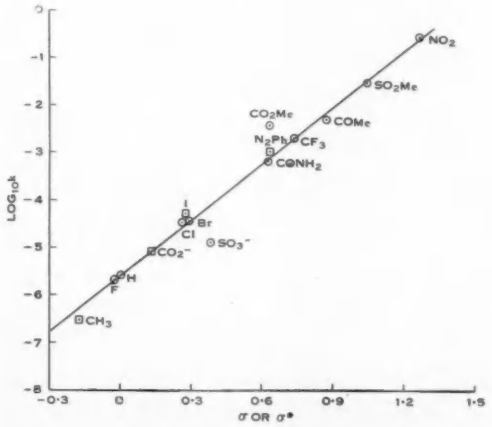

Fig. 2.—4-Substituted 1-chloro-2-nitrobenzenes at 50 °C.
⊙ σ⁺ Values. ⊡ σ Values.

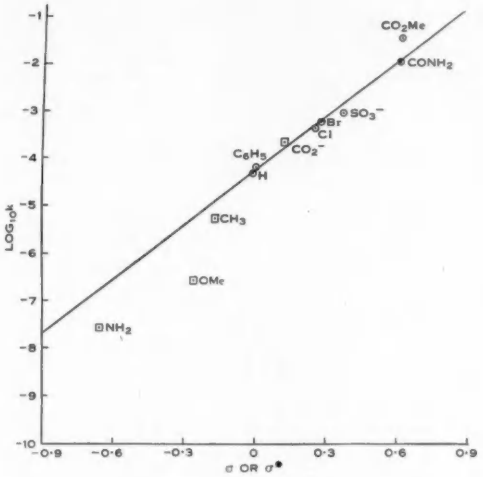

Fig. 3.—4-Substituted 1-chloro-2,6-dinitrobenzenes at 0 °C.
⊙ σ* Values. ⊡ σ Values.

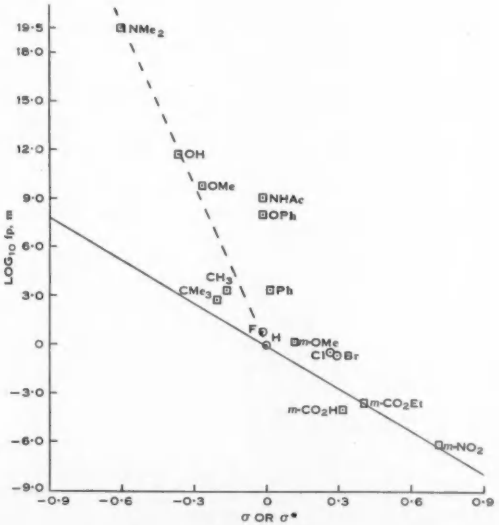

Fig. 4.—Halogenation of benzenes at 25 °C.
⊙ σ* Values. ⊡ σ Values.

III. Discussion

Values of $\log_{10} k$ used in Tables 1 to 3 are obtained from Miller (1951, 1952), Bolto and Miller (1953), Downing, Heppolette, and Miller (1953), Heppolette and Miller (1953), Miller (1954), Heppolette and Miller (1954), Heppolette, Miller, and Parker (1954), Bolto, Liveris, and Miller (1955), Hepploette, Miller, and Parker (1955), and Miller (1955) except where indicated; while the values of σ or σ^* are obtained from Jaffé (1953), except for the following additional values of σ^*: *p*-F $-0{\cdot}015$; *p*-Cl $0{\cdot}265$; *p*-Br $0{\cdot}289$. These are obtained from phenol acidities using the results of Judson and Kilpatrick (1949) and Bordwell and Cooper (1952), and give a good fit to the Hammett equation in Figures 2 and 3. The values of $\log_{10}$ partial rate factor (*para* or *meta*) in Table 4 are obtained from de la Mare and Vernon (1951), Robertson, de la Mare, and Swedland (1953), and de la Mare (1954). By plotting the $\log_{10} k$ against σ or σ^* values, Figures 1 to 4 are obtained, and thus the values of ρ for the reactions concerned. These are as follows, together with values at other temperatures from data not shown: (i) substituted fluorobenzenes with OMe^- in MeOH at 0 °C equals 9·20 (8·31 at 25 °C; 7·55 at 50 °C); (ii) 4-substituted 1-chloro-2-nitrobenzenes with OMe^- in MeOH at 50 °C equals 3·90 (4·59 at 0 °C); (iii) 4-substituted 1-chloro-2,6-dinitrobenzenes with OMe^- in MeOH at 0 °C equals 3·80; and (iv) substituted benzenes with Br_2 or Cl_2 in acetic acid at 25 °C equals $-8{\cdot}82$. In Figure 1 the three points fall reasonably close to a straight line, but the curve was drawn directly through two of them since the third (for H) involves the large extrapolation of 200 °C using the Arrhenius parameters. In accordance with this the fit improves at higher temperatures. In Figures 2 and 3 the curves were drawn using σ^* values only, but ignoring points for CO_2Me, which lie considerably off the line, and for SO_3^- which is also off the line, and for which both reagent-solvent and ionic strength corrections had to be made.

While the total points of Figure 4 cannot be fitted to any single straight line, it is known that (i) simple *meta*-substituents normally fit the Hammett equation well; (ii) the $-I$ $-T$-substituents in Figure 2 and in nitration of substituted benzenes (Jaffé 1953) fit Hammett plots rather well even as *para*-substituents. Since in Figure 4 the few $-I$ $-T$ type substituents in the *meta*-position do fit a straight line this is accepted as the correct one, though admittedly not of a high order of accuracy, and used for discussion of other substituents in terms of divergences from it; these being of the same character as those referred to earlier. The ρ value thus obtained is reasonable in comparison with that for nitration of substituted benzenes (Jaffé 1953), namely, $-8{\cdot}82$ to $-5{\cdot}93$.

The very large substituent effects shown in the nuclear reactions, especially in the case of single activating or deactivating groups (Tables 1–4 and Figures 1 and 4) are indicated by the corresponding ρ values believed to be the highest so far recorded.

Using σ values for *meta*- and σ^* values for *para*-substituents, the S_N plots (Figs. 1–3) show that electron-attracting substituents fit the Hammett plot satisfactorily. The ordinary σ values for weakly conjugative *p*-CO_2^-, I, and Ph fit well also, while the *p*-CH_3 points are also a reasonable fit. However, the

more powerful electron-releasing *para*-substituents OMe and NH_2 deviate considerably, and while their σ values were used in the plot, σ^* values are no better, and were not plotted, but calculated from the base strengths of aniline, *p*-anisidine, and *p*-phenylenediamine as $-0{\cdot}28$ and $-0{\cdot}55$ compared with the σ values $-0{\cdot}26$ and $-0{\cdot}66$. The σ^{**} values calculated with the aid of the ρ value from Figure 3 are $-0{\cdot}596$ and $-0{\cdot}865$.

In Figure 4 neither σ nor σ^* values for the *para*-$+T$-substituents give any sort of agreement with the curve taken from the σ values with *meta*-substituents. This is understandably concerned with the very large $+E$ effects of the six groups with the largest deviations, but the deviations of the halogens, for example, among other deviating groups indicate E effects of a lesser order. The dotted curve on Figure 4 is regarded simply as an expression of some regularity in the deviation. From the value of ρ, obtained in Figure 4, may be derived values of σ^{**}, and it is noteworthy that for the six groups with large E effects the σ^{**} values are about equal to or larger than the σ^* value of a group which must certainly have bigger $+M$ and $+E$ effects than any considered here. This is the *p*-O^- group and σ^* values estimated for it are $-0{\cdot}90$ and $-1{\cdot}07$ (Berliner 1952 from the results of Abichandani and Jatkar 1938; and Tommila 1944).

In comparing deviations in the S_N and S_E reactions, it should be noted that (i) while deviations are concerned with the general $+T$ effects in both series, only the $+M$ effect is concerned in the S_N reactions, while both $+M$ and $+E$ effects are concerned in the S_E reactions, which therefore show larger deviations; (ii) electron-attracting substituents favour increase of acidity of phenols and anilinium ions, used in deriving σ^* values, and such substituents are expected to give reasonable agreement with the Hammett equation using their σ^* values, though better in the S_N reactions.

Second-order conjugative effects of *meta*-substituents are thought to be negligible (cf. de la Mare and Vernon 1951).

The suggestion of Berliner (1952) that a further set of σ values may be necessary for aromatic nuclear substitutions could be amended as follows. In aromatic nuclear substitutions σ^* values are to be used for *para*-substituents having no $+T$ effects, while a (new) set of σ^{**} values are to be used for electron-releasing $+T$ substituents. Further such values must be subdivided according to whether the reaction is S_N or S_E: the latter being more negative and called σ_E^{**}, while the former are called σ_N^{**}.

A value of σ^* is now recorded for the first time for *p*-N_2^+=1·87, and may be compared with the value 0·74 recently recorded for the *p*-NMe_3^+ by Roberts, Clement, and Drysdale (1951), demonstrating very clearly the powerful $-T$ effect of the diazonium ion. Its σ^* value is the highest recorded in the literature.

When using its σ value, F in particular among the halogens, has often shown a marked deviation from Hammett plots. The σ^* value recorded here removes the anomaly, at the same time confirming the $+M$ effect (Dippy and Lewis 1936; Baker and Hopkins 1949; Heppolette and Miller 1953). An additional $+E$ effect in S_E reactions is shown by the need for a σ_E^{**} value. Similar considerations apply to the other halogens. The value for F in the S_N reactions could be regarded perhaps as a σ_N^{**} value, since a $+M$ effect is involved, and F is

very slightly electron releasing; however, the other halogens are electron attracting and it seems more convenient to group the halogens together. Since the CO_2^- group is scarcely activating, and the $-T$ effect therefore small, the normal σ value fits the Hammett plot well. The other COX groups have considerable $-T$ effects, but the σ^* values in the literature are a good fit to the plot, except for CO_2Me. Jaffé (1953) lists the σ^* for this group as $0{\cdot}636 \pm 0{\cdot}080$, and with an upper limit recorded $=0{\cdot}765$. This latter value would fit Figures 2 and 3 well, and is thus supported. The σ^* value of $0{\cdot}239$ for the $CH{=}CH{-}CO_2^-$ indicates a definite $-T$ effect of the multiple bond in aromatic S_N reactions.

The deviation of the CH_3 group is small but definite, and illustrative of hyperconjugation. The values $-0{\cdot}170$; $-0{\cdot}237$ and $-0{\cdot}256$; and $-0{\cdot}374$ for σ, σ_N^{**}, and σ_E^{**} respectively, indicate magnitudes for $+M$ and $+E$ components of the hyperconjugation. The lower σ_E^{**} for CMe_3 is probably significant.

The σ^* values for the SO_2X groups all confirm the powerful $-T$ effect already indicated by the provision of a σ^* value in the literature (Jaffé 1953) for SO_2Me. Even the SO_3^- group shows a value significantly larger than for CO_2^-, a trend well shown by comparing corresponding COX and SO_2X values. The new σ^* values are for SO_2NMe_2 and SO_2Ph.

In the S_N reactions the σ value for Ph fits the Hammett plot well, though a σ^* value is calculated, and indicates that the second ring operates almost entirely by a small $(-I)$ inductive effect. In contrast a σ_E^{**} value of some magnitude and in the opposite direction is required, so that in the S_E reactions the ring exerts a definite $+T$ effect also.

The σ_N^{**} values for OMe and NH_2 are considerably more negative than recorded values of σ; or σ^* values as calculated from amine basicities (see earlier). Jaffé (1953) does not list the precision of σ values for those two but does for the closely similar OH and NMe_2, namely, p-OH $= -0{\cdot}357 \pm 0{\cdot}104$ with limits $-0{\cdot}208$ to $-0{\cdot}694$; p-$NMe_2 = -0{\cdot}600 \pm 0{\cdot}213$ with limits $-0{\cdot}206$ to $-1{\cdot}049$. However, the cases giving the lower limit values, which are approximately the same numerically as the σ_N^{**} values given here, are discussed briefly by Jaffé as being cases where resonance interactions are very strong, and thus different from the normal σ values. He regards them as analogous to the σ^* values, his argument being in terms of strong interaction of electron-withdrawing and electron-releasing side chains. This corresponds to measurements of phenol and aniline strengths for electron-attracting substituents, but not for electron-releasing substituents, and the analogy is therefore to σ_N^{**} values as calculated here, and not to σ^* values. The σ_E^{**} values which take into account also very large $+E$ effects are completely out of the range even of the special cases listed by Jaffé; thus p-$NMe_2 = -2{\cdot}211$; p-OH $= -1{\cdot}338$. One other group listed by Jaffé may be quoted — p-OPh with $\sigma = -0{\cdot}028 \pm 0{\cdot}080$ with limits $+0{\cdot}118$ to $-0{\cdot}109$, while the σ_E^{**} value is $-0{\cdot}896$.

While precisions of the literature values are unknown many other electron-releasing groups recorded in this paper have σ_E^{**} values very different from recorded σ values.

The σ value for N_2Ph gives quite a good fit in Figure 2 suggesting that the activating power of the group is due almost entirely to the inductive ($-I$) effect, although a small $-T$ effect would be expected. In S_E reactions also the group is activating but only weakly (de la Mare and Vernon 1951), and comparison with amino groups illustrates the marked difference in electronegativity between single and multiple bonded nitrogen, analogous to that in the more extended sequence from single to triple bonded carbon.

The rates recorded in the references already used for discussion of the Hammett equation may also be used to attempt a direct comparison of individual substituent effects in aromatic nuclear S_N and S_E reactions. In making this comparison the following features should be borne in mind:

(i) Substituents which exhibit an M effect in one series will exhibit both M and E effects in the other (Ingold 1953, pp. 64, 88).

(ii) Similarly, substituents which exhibit an I_s effect in one series will exhibit both I_s and I_d effects in the other (Ingold 1953, p. 72). This is rarely important compared with (i), but may be so in the alkyl groups where conjugative effects are small.

(iii) Both absolute and relative magnitudes of substituent effects depend on the electron requirements of the reagent, and on the presence of other substituents. Brown and Nelson (1954) give a useful table illustrating the former, and the ρ values of Figures 1 and 2 demonstrate the latter (cf. Bolto, Liveris, and Miller 1955).

(iv) The nature of aromatic compounds with an external π-electron "cloud" implies that benzene, and substituted benzenes with weakly polar substituents, are more susceptible to electrophilic than nucleophilic attack. It also suggests that superposition of substituent effects for S_E reactions will be more facile than for S_N reactions, where any considerable activation requires a marked denudation of the π-electron cloud to expose an electron-deficient ring carbon atom to attack (cf. Ingold 1953, p. 798). It is perhaps relevant to note that simple aromatic compounds, even when containing displaceable atoms or groups which readily form anions (e.g. F and the halogens generally) react very slowly with most nucleophilic reagents (cf. Bolto, Liveris, and Miller 1955), but react fairly readily with a considerable range of electrophilic reagents.

Comparison of substituent effects is made in Table 5 in which a few unpaired values are given to show as far as possible the overall scale of substituent effects.

The important part played by T effects is well shown by the results for OMe and NH_2 in electrophilic, and NMe_3^+, NO_2, and N_2^+ in nucleophilic substitution. It is also relevant that the results of Bonner *et al.* (1949) show that the NMe_3^+ is more deactivating than the NO_2 group in an aromatic S_E reaction (nitration) so that the reverse situation in the S_N reaction further confirms the importance of the T effect.

TABLE 5

COMPARATIVE SUBSTITUENT EFFECTS FOR S_E AND S_N REACTIONS

Substituent	Electronic Effect	Reaction Type	Reagent	Temp. (°C)	Partial, S_E, or Substituent, S_N, Rate Factor	References
p-N_2^+	$-I$ $-T$	S_N	OMe⁻	0	$1{\cdot}68\times10^{16}$	(a)
p-NO_2	$-I$ $-T$	S_N	OMe⁻	0	$6{\cdot}20\times10^{10}$	(a)
				50	$1{\cdot}33\times10^{9}$	
p-NO_2 (Cl displaced group)	$-I$ $-T$	S_N	OMe⁻	0	$6{\cdot}73\times10^{5}$	(b)
				50	$1{\cdot}14\times10^{5}$	
p-NO_2 (Br displaced group)	$-I$ $-T$	S_N	OMe⁻	0	$1{\cdot}14\times10^{6}$	(b)
				50	$1{\cdot}01\times10^{5}$	
p-NMe_3^+ ..	$-I$	S_N	OMe⁻	0	$3{\cdot}85\times10^{4}$	(a)
				50	$1{\cdot}43\times10^{4}$	
m-NO_2	$-I$ $(-T)$	S_N	OMe⁻	25	$1{\cdot}65\times10^{5}$	(c)
m-NO_2	$-I_s$ $(-M)$	S_E	Br_2	25	$8{\cdot}9\times10^{-7}$	(d)
p-CO_2Me ..	$-I$ $-T$	S_N	OMe⁻	25	$3{\cdot}15\times10^{2}$	(e)
p-CO_2Et ..	$-I_s$ $-M$	S_E	NO_2X	18	9×10^{-4}	(f)
p-N_2Ph ..	$-I$ $-T$	S_N	OMe⁻	25	$6{\cdot}37\times10^{2}$	(g)
p-N_2Ph ..	$-I_s$ $+T$	S_E	Cl_2	25	4·6 (relative rate)	(d)
p-Ph	$-I$ $-T$	S_N	OMe⁻	25	1·44	(h)
p-Ph	$-I_s$ $+T$	S_E	Br_2	25	$2{\cdot}5\times10^{2}$	(d)
p-F	$-I$ $+M$	S_N	OMe⁻	25	$8{\cdot}08\times10^{-1}$	(c)
p-F	$-I_s$ $+T$	S_E	Cl_2	25	6·3	(d)
p-Cl	$-I$ $+M$	S_N	OMe⁻	25	$1{\cdot}59\times10^{1}$	(c)
p-Cl	$-I_s$ $+T$	S_E	Cl_2	25	$4{\cdot}0\times10^{-1}$	(d)
p-Cl	$-I_s$ $+T$	S_E	NO_2X	18	$1{\cdot}4\times10^{-1}$	(i)
p-Br	$-I$ $+M$	S_N	OMe⁻	25	$1{\cdot}37\times10^{1}$	(c)
p-Br	$-I_s$ $+T$	S_E	Cl_2	25	$2{\cdot}5\times10^{-1}$	(d)
p-Br	$-I_s$ $+T$	S_E	NO_2X	18	$1{\cdot}1\times10^{-1}$	(i)
p-I	$-I$ $+M$	S_N	OMe⁻	25	$1{\cdot}66\times10^{1}$	(c)
p-I	$-I_s$ $+T$	S_E	Cl_2	25	$1{\cdot}8\times10^{-1}$ (relative rate)	(d)
p-OMe ..	$-I$ $+M$	S_N	OMe⁻	25	$1{\cdot}10\times10^{-2}$	(j)
p-OMe ..	$-I_s$ $+T$	S_E	Br_2	25	$6{\cdot}3\times10^{0}$	(d)
p-NH_2 ..	$-I$ $+M$	S_N	OMe⁻	25	$8{\cdot}09\times10^{-4}$	
p-NMe_2.. ..	$-I_s$ $+T$	S_E	Br_2	25	$3{\cdot}2\times10^{19}$	(j)
p-CH_3	$+I_s$ $+M$	S_N	OMe⁻	25	$1{\cdot}42\times10^{-1}$	(d)
				50	$1{\cdot}19\times10^{-1}$	(k)
p-CH_3	$+I$ $+T$	S_E	Br_2	25	$2{\cdot}0\times10^{2}$	
p-CH_3	$+I$ $+T$	S_E	NO_2X	45	$5{\cdot}8\times10^{1}$	(d)
p-CMe_3 ..	$+I(+T)$	S_E	Br_2	25	$6{\cdot}3\times10^{2}$	(l), (m)
p-CMe_3 ..	$+I(+T)$	S_E	NO_2X	45	$7{\cdot}5\times10^{1}$	(d)
m-O^-	$+I_s(+M)$	S_N	OMe⁻ (calc.)	0	$1{\cdot}44\times10^{-5}$	(l)
				50	$2{\cdot}88\times10^{-5}$	(j)

(a) Bolto, Liveris, and Miller (1955). (b) Beckwith, Miller, and Leahy (1952); Bolto, Miller, and Williams (1955). (c) Heppolette and Miller (1953). (d) de la Mare and Vernon (1951); Robertson, de la Mare, and Swedlund (1953); de la Mare (1955). (e) Miller (1954). (f) Ingold and Smith (1938). (g) Heppolette, Miller, and Parker (1954). (h) Bolto and Miller, unpublished data. (i) Bird and Ingold (1938). (j) Liveris *et al.* (1955). (k) Heppolette Miller, and Williams (1955). (l) Cohn *et al.* (1952). (m) Ingold *et al.* (1931).

The similarity in *magnitude* of the substituent effects of the halogens in both S_N and S_E reactions demonstrates the major role in that group of the I effects as regards the level of reactivity.

The N_2Ph and the Ph groups are the only ones among those considered which have a different *directional* classification of electronic effects in the two series, so that these groups are activating in both S_N and S_E reactions.

The extreme range of *para*-substituents considered in the S_N reactions is from a very powerfully activating $-I$ $-T$ cation (N_2^+) to a powerfully deactivating electrically neutral group (NH_2). Measurements for the latter were made in a less sensitive series and an allowance was made by using the relative ρ values from Figures 1 and 3. The range of substituent rate factors (substituted fluorobenzenes with OMe^- in MeOH at 25 °C) then becomes about 5×10^{22}. In the S_E reactions a much less extreme range of *para*-substituents has been measured, namely, from a powerfully activating electrically neutral group (NMe_2) to a moderately powerful electrically neutral deactivating group (CO_2Et). Again, allowing for a difference in sensitivity of reaction by utilizing the relative ρ values for bromination (from Fig. 4) and nitration (Jaffé 1953) the range of partial rate factors is found to be about 10^{24} (for bromination of substituted benzenes in acetic acid at 25 °C).

The S_N and S_E series thus compared have very similar ρ values, so that the difference lies in the σ values, and more particularly in the differences between σ_N^{**} and σ_E^{**} values introduced in this paper as an extension to σ and σ^* values. The result is nevertheless unusual and is really a consequence of the function of the σ^{**} values in attempting to allow for a breakdown of the normal Hammett relationship. A legitimate alternative would be to define different ρ values for electron-attracting and electron-releasing substituents for aromatic *nuclear* S_N and S_E reactions. However, this is not otherwise discussed here since, as indicated, the use of σ^{**} values is simply an extension of the generally accepted introduction of σ^* values.

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THE S_N MECHANISM IN AROMATIC COMPOUNDS

XVII. CATIONIC REPLACED GROUPS IN AROMATIC S_N REACTIONS

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Summary

The general order of ease of displacement in activated aromatic S_N reactions—cation > dipole > neutral group is confirmed. The special place of F among electrically neutral groups is noted and the experimental order $SMe_2^+ > NMe_3^+ > F > \overset{+}{N}O_2^- > Cl$ is discussed.

I. Introduction

Some early work on variation of replaced groups in aromatic nucleophilic substitution by a Dutch group (e.g. Lulofs 1901 ; Steger 1899, 1904) has been considerably augmented in recent years (e.g. Bunnett and Levitt 1948 ; Ogata and Okano 1949 ; Bevan 1951 ; Beckwith, Miller, and Leahy 1952 ; Berliner and Monack 1952 ; Briner *et al.* 1954 ; Chapman, Parker, and Soames 1954 ; Bolto, Miller, and Williams 1955). The kinetic work on replaced groups has dealt only with replacement of electrically neutral groups, except in one case dealing with a replacement of the dipolar NO_2 group at one temperature.

Bunnett and Zahler (1951) in their review quote without explanation an order of replacement $F > NO_2 > Cl,Br,I > NR_3^+$. One of us (Miller 1951) in a review has discussed briefly the effect of varying the replaced group, and given the general order $ArX^+ > ArX > ArX^-$, and the specific order $F > Cl > Br > I$. While dipolar groups were not specifically mentioned, the discussion given would lead to the order $ArX^+ > Ar\overset{+}{X}\overset{-}{Y} > ArX$, which the present paper is partly intended to confirm.

Since the most commonly displaced group in aromatic S_N reactions is Cl, Bolto, Miller, and Williams (1955) have defined a group replacement factor (G.R.F.) as the comparative rate of displacement $ArX/ArCl$ at a given temperature. Tables 1 and 2 list rate constants and derived quantities, including the G.R.F.'s, for replacement of X in a series p-$NO_2C_6H_4X$ by OMe^- in MeOH (absolute), where X equals (i) Cl, (ii) F, (iii) NO_2, (iv) $NMe_3^+Cl^-$, and (v) $SMe_2^+MeSO_4^-$.

The extraordinary ease of replacement of F compared with the other halogens, themselves among the more easily displaced neutral groups, makes the position of F unique among such groups : it is, for example, considerably

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TABLE 1

Compound	Replaced Group	Rate Constant, k_2 ($l\,mole^{-1}\,sec^{-1}$)					
		At Temperatures (°C) in Parentheses			Calculated at 0 °C	Calculated at 50 °C	Calculated at 100 °C
(i)	Cl	Previously recorded (Briner *et al.* 1954)			$8{\cdot}90\times10^{-9}$	$8{\cdot}47\times10^{-6}$	$1{\cdot}28\times10^{-3}$
(ii)	F	Previously recorded (Briner *et al.* 1954)			$6{\cdot}26\times10^{-6}$	$2{\cdot}64\times10^{-3}$	$2{\cdot}21\times10^{-1}$
(iii)	NO_2	$1{\cdot}68\times10^{-4}$ (25·1)	$5{\cdot}95\times10^{-4}$ (35·6)	$1{\cdot}91\times10^{-3}$ (45·45)	$5{\cdot}21\times10^{-6}$	$3{\cdot}11\times10^{-3}$	$3{\cdot}34\times10^{-1}$
(iv)	NMe_3^+	$6{\cdot}03\times10^{-4}$	$1{\cdot}77_5\times10^{-3}$	$4{\cdot}37\times10^{-3}$	$3{\cdot}08\times10^{-5}$	$7{\cdot}23\times10^{-3}$	$3{\cdot}93\times10^{-1}$
		[$1{\cdot}54\times10^{-3}$]*	[$4{\cdot}41\times10^{-3}$]	[$1{\cdot}21\times10^{-2}$]	[$6{\cdot}66\times10^{-5}$]	[$2{\cdot}00\times10^{-2}$]	[$1{\cdot}30\times10^{0}$]
		(25·2)	(35·3)	(44·7)			
(v)	SMe_2^+	$9{\cdot}77\times10^{-4}$	$3{\cdot}70\times10^{-3}$	$1{\cdot}59\times10^{-2}$	$4{\cdot}12\times10^{-4}$	$3{\cdot}46\times10^{-1}$	$4{\cdot}79\times10^{1}$
		[$3{\cdot}94\times10^{-3}$]	[$1{\cdot}57\times10^{-2}$]	[$7{\cdot}17\times10^{-2}$]	[$1{\cdot}60\times10^{-3}$]	[$1{\cdot}77\times10^{0}$]	[$2{\cdot}97\times10^{2}$]
		(5·55)	(14·6)	(25·0)			

* Values in [ ] corrected to zero ionic strength.

more readily displaced than even the 2,4-dinitrophenoxy group (Beckwith and Miller, unpublished data). The results may therefore be taken as illustrating clearly the order cation>dipole>neutral group; the order $NMe_3^+ > \overset{+}{N}\overset{-}{O}_2 > NR_2$ being implicit since the difficulty of replacing amino groups in comparison with Cl is well known.

The predicted orders are based on electronegativity rather than bond strength considerations (Miller 1951; Beckwith, Miller, and Leahy 1952; Briner *et al.* 1954; Bolto, Miller, and Williams 1955), and the present results taken with the earlier ones suggest that for attack by a reagent such as OMe^- on an activated molecule bond breaking is not relevant to the rate determining step, though bond weakening in the change from $Ar-X$ to $Alph-X$ type of bonding is presumably involved to some extent. In the attack by anionic reagents electrostatic considerations are thought to play an important part

TABLE 2

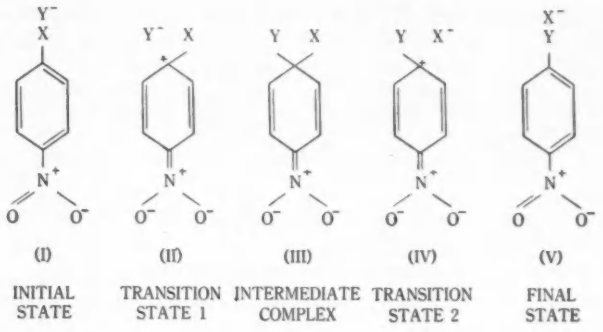
Compound	Replaced Group	Group Replacement Factor at 0 °C	50 °C	100 °C	Activation Energy, E (calc.)	Frequency Factor, $\log_{10} B$
(i)	Cl	1	1	1	240_{50}	11·2
(ii)	F	$7{\cdot}03\times10^2$	$3{\cdot}12\times10^2$	$1{\cdot}72\times10^2$	21200	$11{\cdot}7_5$
(iii)	NO_2*	$2{\cdot}93\times10^2$	$1{\cdot}83\times10^2$	$1{\cdot}30\times10^2$	22400	$12{\cdot}6_5$
(iv)	NMe_3^+	$7{\cdot}48\times10^3$	$2{\cdot}36\times10^3$	$1{\cdot}02\times10^3$	20000†	11·8†
(v)	SMe_2^+	$1{\cdot}80\times10^5$	$2{\cdot}09\times10^5$	$2{\cdot}32\times10^5$	245_{50}†	$16{\cdot}8_5$†

* For statistical reasons the G.R.F. for this compound is taken as *half* the rate ratio.
† Obtained using rate constants corrected to zero ionic strength.

therefore in the formation of the transition state. It is generally held that a fully bonded intermediate complex with quinonoid type structure is also involved in aromatic substitution (e.g. Miller 1951; Ingold 1953; Brown and Nelson 1954; Hammond 1955) and one may write tentatively the following sequence I to V for the change from initial to final state, in which it is to be understood that the dipolar quinonoid type structure approximates only the transition states II and IV (each of which has also one electrostatic type bond), since the extent of change from benzenoid to the extended *cyclo*pentadienide (or quinonoid) type conjugation, accompanied by a change from $Ar-X$ to $Alph-X$, is unknown. It will in fact vary with the electronegativity of X, the nucleophilicity of the reagent, and extent and type of substituents present. For reactive compounds the loss of X to form X^- (sign being relative) is a facile process so that the potential energy of the second transition state is lower than that of the first. The corresponding potential energy-reaction coordinate diagram is shown as Figure 1.

For reaction with electrically neutral reagents, particularly those which are weakly nucleophilic, the transition states much more resemble the intermediate complex, both structurally and energetically. Thus bond breaking becomes

relevant to the rate determining step; and particularly so when a poorly solvating reaction medium is used, so that the final formation of an anion and cation is energetically unfavourable, and the potential energy of the second transition state may be higher than the first. This situation has been particu-



larly discussed by Hammond (1955), but it should be noted that in behaviour such aromatic nucleophilic substitutions resemble those of the aliphatic series, in which there is but one transition state, and no intermediate complex. Chapman, Parker, and Soames (1954, and earlier papers) do treat such reactions for convenience as quasi-aliphatic in this sense.

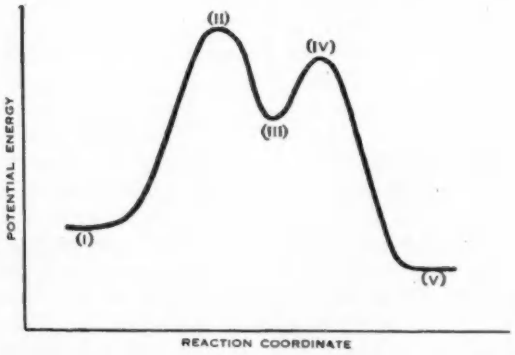


Fig. 1.—Typical P.E. diagram for activated aromatic nucleophilic substitutions.

The difference between the two extremes discussed is well illustrated by comparison of the G.R.F. of F when 1-fluoro-2,4-dinitrobenzene is reacted with (i) a moderately nucleophilic anionic reagent in a good solvating medium (Beckwith, Miller, and Leahy 1952); and (ii) a weakly nucleophilic neutral

reagent in a poor solvating medium (Hammond 1955). The change in G.R.F. is of the order of 10^4.

It is readily seen from the above discussion that displacement of cationic, and to a lesser extent, dipolar groups is specially facile; and with the various intermediates shown that (1) there will be no relation between ease of replacement and nucleophilicity (or basicity) of the group when in its displaced form (one unit more negative) (2) bond strength factors will not be involved, except in the change from Ar—*X* to Alph—*X* type bonding.

While the discussion suffices for the gross differences between cationic, dipolar, and neutral groups, and between F and the other halogens, more explicit discussion is required to explain the difference between the SMe_2^+ and NMe_3^+ groups.

From what has already been said, ordinary bond strength factors are not expected to be involved, and it seems unlikely in any case that the C—S^+ bond is weaker than the C—N^+ bond (Bolto and Miller 1955).

Models of NMe_3^+ and SMe_2^+ attached to the benzene ring show that the C atom of the Ar—N^+ bond is comparatively inaccessible to the reagent while that of the Ar—S^+ bond is readily accessible. However, there might be some repulsive influences between the *N*-methyl groups and the π-electrons of the ring, thus facilitating replacement of the NMe_3^+ by relief of strain.

Partial double bond formation is likely for the Ar—S^+ bond due to the ability of S to expand its outer shell to more than an octet. This is not possible in the Ar—N^+ bond, and thus for the former only, a bond weakening factor is relevant to the rate determining step. The conjugative effect mentioned stabilizes particularly the initial state, and this is consistent with the near identity of activation energy for the sulphonium as compared with the chloro-compound. The very high frequency factor is to be expected for the reaction between an anion and a cation to which the reagent has ready access. In the case of the ammonium ion it appears that steric factors cancel the effect of positive charge in raising the frequency factor, while the absence of initial state stabilization may account for the comparatively low value of the activation energy.

The above discussion is tentative, but if valid would lead to the conclusion that the Arrhenius parameters for the F and NO_2 compounds would lie between those for Cl and SMe_2^+, and not resemble those for NMe_3^+; and this is found experimentally.

Rate constants for the reaction of an anion with a cation (the sulphonium compound) were measured at different ionic strengths at one temperature and thus extrapolated to zero ionic strength, and by a method discussed in Section II, values for zero ionic strength at other temperatures obtained and then used to obtain the Arrhenius parameters.

In view of the similarity in shape of the ammonium and sulphonium ion the same correction constants were used for the former also. The corrections were of a magnitude such that discussion based on ignoring ionic strength

effects was in no way affected. No corrections were made for the reaction of the anion with the molecule with a dipolar replaced group (*p*-dinitrobenzene) and this is justified by the experimental results of Steger (1899, 1904).

II. Experimental

While measurements of the rate constants of the sulphonium compound can be followed in the usual way by acid-base titrations, after stopping the reaction in dilute HCl, this method is not available for the ammonium ion since OMe^- is replaced by Me_3N which is a moderately strong base (though weak nucleophile; Lantzke and Miller, unpublished data). A conductimetric procedure was evolved, and is discussed below. In the reaction with *p*-dinitrobenzene some difficulty was expected with runs, but it was found that reproducible results could be obtained by stopping reaction with dilute acetic acid and titrating with phenolphthalein as indicator. A later check by potentiometric methods confirmed the results, but for this compound results were of a lesser order of accuracy than is usually obtainable.

Conductimetric procedure: the reaction is

$$p\text{-}NO_2C_6H_4NMe_3{}^+Cl^- + Na^+OMe^- \rightarrow p\text{-}NO_2C_6H_4OMe + Na^+Cl^-.$$

It is assumed that in the dilute solutions used (about 0·01M instead of the usual initial concentration of 0·05M) the various ionic conductances remain sensibly independent of the presence of other ions. As reaction proceeds the conductance of the solution decreases due to the disappearance of two of the four ions. By measuring at each temperature the conductance in the experimental range of $p\text{-}NO_2C_6H_4NMe_3{}^+Cl^-$; Na^+OMe^-; Na^+Cl^- it was possible to obtain a calibration curve of conductance versus concentrations for the reacting ions by the equation

$$\lambda_{p\text{-}NO_2C_6H_4NMe_3{}^+OMe^-} = \lambda_{p\text{-}NO_2C_6H_4NMe_3{}^+Cl^-} + \lambda_{Na^+OMe^-} - \lambda_{Na^+Cl^-},$$

at the appropriate concentrations.

Equimolar starting concentrations of reagent and reactant were used, the exact concentration being obtained by estimation of Cl^- at the end of reaction. In using the measured conductance values it was necessary in each case to subtract the conductance of the constant amount of Na^+Cl^-.

(*a*) *Typical Kinetic Results*

A typical kinetic run (for the sulphonium compound at 14·6 °C) is shown as Table 3, and the graphical value compared with that obtained by least squares. Similarly Table 4 gives a typical conductimetric run (the ammonium compound at 35·3 °C). Neither is corrected to zero ionic strength. Table 5 shows the full set of rate constants already corrected to zero ionic strength as used to determine the activation energy by a least squares analysis of the values of $\log k_2$ and reciprocal temperature for one compound (the sulphonium ion). The " probable errors " thus obtained for the Arrhenius parameters are less than the estimated errors of up to $\pm$350–400 in E, and about $\pm$0·3 in $\log_{10} B$.

TABLE 3
SULPHONIUM ION AT 14·6 °C

Titre	Log Term	Time (min)
16·01	0·1536	0
16·24	0·1593	5
16·51	0·1665	10
16·90	0·1783	21
17·21	0·1889	30
17·65	0·2064	45
18·01	0·2234	60
18·43	0·2472	80
18·81	0·2737	100
19·18	0·3058	130
21·43 (av. of 3)	—	∞

k_2 (graph) $= 3 \cdot 67 \times 10^{-3}$
k_2 (least squares) $= 3 \cdot 69_0 \pm 0 \cdot 01_7 \times 10^{-3}$ (l mole^{-1} sec^{-1})

TABLE 4
AMMONIUM ION AT 35·3 °C

Resistance, ω	Reciprocal Term	Time (min)
325	102·1	0
331	106·0	30
335	108·5	60
338	110·3	90
342	113·3	120
348	117·2	150
353	120·8	180
357	124·5	200
361	127·4	230
371	136·2	300
372	137·0	330
377	141·8	360
381	145·3	390
382	146·6	420
386	150·8	465

k_2 (graph) $= 1 \cdot 81 \times 10^{-3}$
k_2 (least squares) $= 1 \cdot 80_9 \pm 0 \cdot 02_2 \times 10^{-3}$ (l mole^{-1} sec^{-1})

TABLE 5
SULPHONIUM ION

$10^5 k_2$ (l mole^{-1} sec^{-1}) ..	390	398	1555	1590	7140	7210
Temperature (°C) ..	5·55	5·55	14·6	14·6	25·0	25·0

E (least squares) $= 24550 \pm 110$ cal.; reported as 245_{50}
$\log_{10} B$ (least squares) $= 16 \cdot 86 \pm 0 \cdot 08$; reported as $16 \cdot 8_5$

By the Bronsted equation the reaction between ions of unlike charge is given by

$$\log k = \log k_0 + 2Az_Az_B\sqrt{(\mu)},$$

where k=rate constant,

$z_{A,B}$=unit charges of anion and cation,

A=Debye constant,

$$=\frac{N^2\varepsilon^3\sqrt{(\pi/500)}}{2\cdot3026(RDT)^{3/2}}=1\cdot862 \text{ (for MeOH at 20 °C)},$$

N=Avogadro's number,

ε=electronic charge,

R=gas constant,

D=dielectric constant,

T=absolute temperature,

μ=ionic strength.

Using the value of Jones and Davies (1939) for D for MeOH at 20 °C=33·57 the Bronsted equation becomes

$$\log k = \log k_0 - 3\cdot724\sqrt{(\mu)}.$$

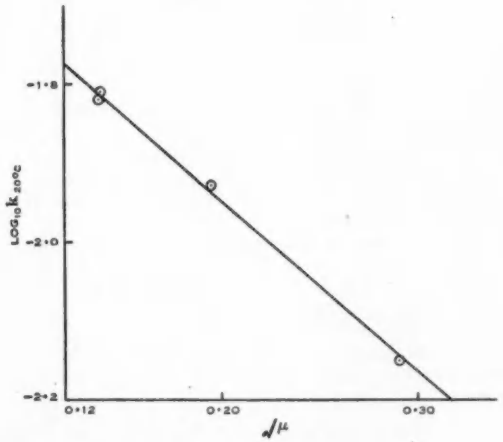


Fig. 2.—Rate constant and ionic strength relationship (p-nitrophenyldimethylsulphonium methosulphate at 20 °C).

Rates were determined for the sulphonium compound experimentally at three ionic strengths. The plot of $\log k_{20\,°C}$ against $\sqrt{(\mu)}$ (initial) was a good straight line (Fig. 2) but with gradient $2\cdot20_9\pm0\cdot02_9$, and with $k_{20\,°C}=3\cdot11_9\pm0\cdot02_9\times10^{-2}$. There are three likely contributory reasons for the difference of gradient from theory: (i) the cation is not spherical, (ii) the positive charge is not at the reaction centre, (iii) the ionic strength decreases during reaction. The effect of (i) is thought to be small, while (ii) and (iii) result in the ionic strength correction being smaller than that given by simple theory, as is found.

The Debye constant A may be rewritten as $B/(DT)^{3/2}$, where B is a temperature independent term. Using values of D for MeOH at 5, 15, and 25 °C (Albright and Gosting 1946) it was possible to obtain k at zero ionic strength for all the experimental temperatures. In a similar way, using values of D at 25, 35, and 45 °C (Albright and Gosting 1946) corrected values for the ammonium ion were also calculated.

(*b*) *Preparation of Materials*

p-Chloronitrobenzene and *p*-fluoronitrobenzene: as by Briner *et al.*'s (1954) method.

p-Dinitrobenzene: the commercial product was recrystallized from ethanol to constant m.p. 173–174 °C (lit. 171·5–172 °C; 173·5 °C).

p-Nitrophenyltrimethylammonium chloride and *p*-nitrophenyldimethylsulphonium methosulphate: as by the method of Bolto and Miller (1955).

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THE CHEMISTRY OF PYRIDINE, PYRIMIDINE, AND PYRAZINE

By R. D. Brown* and M. L. Heffernan*

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Summary

The results of a study of pyridine, pyrimidine, and pyrazine by the molecular-orbital method are reported, and a detailed comparison is made with the chemical properties of these molecules. Good agreement is found, indicating that the present theoretical technique is satisfactory for interpreting and predicting the chemical properties of nitrogen heterocycles.

I. Introduction

In a previous paper (Brown 1955) the simple molecular-orbital approximation, ignoring overlap, was tested by making a detailed comparison of the theoretical results for five-membered ring nitrogen heterocycles with the known chemistry of these compounds. This investigation of the molecular-orbital theory is continued here by studying six-membered ring nitrogen heterocycles. Some previous theoretical attention has been given to these heterocycles, particularly to pyridine (Yvan 1949; Sandorfy and Yvan 1950; Longuet-Higgins and Coulson 1947; Löwdin 1951). These earlier calculations were performed using values for the heterocycle parameters which are now known to be unsatisfactory (see below) and the comparison with experiment was not as thorough as is now desirable. Calculations for the other heterocycles have been reported (Orgel *et al.* 1951; Davies 1955) but in neither case was the prime aim the comparison of the results with chemical properties, so that the localization energies were not computed, thus leaving some uncertainty about the validity of the non-crossing rule (Brown 1952) and hence about the comparison with chemical properties. In addition the values used by these workers for the heterocycle parameters have now been shown (Brown 1956) to differ somewhat from the optimum values for treatment of chemical properties.

Previously it has not been sufficiently recognized that for reactions occurring in acidic media the heterocycles are present as their conjugate acids in which the nitrogen atoms carry formal positive charges and so are much more electronegative than they are in the free bases. We have therefore performed the calculations for two different values of the electronegativity parameter, one corresponding to the electronegativity for the free base, and a larger value which we hope will give a reasonable representation of the electronic situation in the conjugate acids. Results for other electronegativity values could be roughly assessed by interpolation between the two sets of results if this subsequently proves to be necessary.

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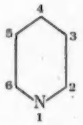
The two values adopted for the relative electronegativity parameter h (Brown 1955) were $+0\cdot5$, which is appropriate for the free bases (Brown 1956), and $+2\cdot0$, which we judge to be reasonable for protonated nitrogen atoms.*

The resonance integrals of all bonds were assigned the standard value β. This is the optimum value for β_{CN} (Brown 1956) as well as for β_{CC}.

With these assumed values we have computed charge densities q, free valences F, and atom localization energies A, for all three types of substitution reactions, namely, electrophilic, homolytic, and nucleophilic.

II. Results and Discussion

The theoretical results for pyridine (I) are presented in Table 1. For electrophilic substitution both the π-electron densities and the localization energies A_e predict that the 3-position will have the highest reactivity in the free base and in the conjugate acid. Furthermore at this position the electronic



(I)

situation is very similar to that at an ordinary benzene position (charge density $=1$ and $A_e=-2\cdot536\beta$), although the localization energy for the 3-position of the conjugate acid indicates a somewhat lower reactivity than for a benzene position.

Table 1

THEORETICAL RESULTS FOR PYRIDINE POSITIONS

h	Position	A_e $(-\beta)$	A_r $(-\beta)$	A_n $(-\beta)$	q*	F†
0·5	2	2·6718	2·5124	2·3529	0·923	0·399
	3	2·5381	2·5381	2·5381	1·004	0·398
	4	2·7011	2·5374	2·3737	0·950	0·402
2·0	2	2·7087	2·2838	1·8588	0·759	0·515
	3	2·5604	2·5604	2·5604	1·012	0·488
	4	3·0711	2·5418	2·0125	0·835	0·438

* π-Electron density.

† Free valence (max. bond No. 1·732).

Experimentally, it is well established that electrophilic substitutions producing nitration (Kirpal and Reiter 1925), halogenation (Wibaut and Nicolai 1939 ; Wibaut and den Hertog 1945), and sulphonation (Fischer 1882 ; McElvain and Goese 1943) take place in the 3-position. The very low reactivity of the heterocycle observed in these reactions is to be attributed to the inherent reluctance of two cations to collide rather than to π-electron effects.

* This is probably an overestimate of h but we feel that this is safer than a smaller value which might subsequently prove to be an underestimate and so call for extrapolation of our results.

For nucleophilic attack both π-electron densities and localization energies predict that the order of reactivity of the positions is 2>4>3. Experimentally, it is found that the amination of pyridine takes place mainly in the 2-position (Leffler 1941), but it is not yet certain that amination proceeds by a nucleophilic substitution mechanism (Badger 1954). The mechanism proposed for amination (Ingold 1953) may be extended to the reaction with lithium aryls (Evans and Allen 1943). This converts pyridine to 2-aryl derivatives. Finally, the hydroxylation of pyridine yields largely 2-hydroxypyridine (Tschitschibabin 1923). That the orientations observed in these reactions are those predicted for a heterolytic mechanism may be regarded as indirect evidence for the mechanisms of these reactions.

A low π-electron density at a carbon atom produces an enhanced acidity of an attached methyl group by an inductive electron drift. Thus from the theoretical results we should expect the reactivities of the picolines with reagents such as benzaldehyde to be in the order 2>4>3. Experimentally, it is known that α-picoline and to a lesser extent γ-picoline, but not the β-isomer, react with aromatic aldehydes (Baurath 1887 ; Ladenburg and Kroener 1903 ; Shaw and Wagstaff 1933).

It has recently been shown (Brown 1956) that the localization energies A are in excellent agreement with the observed partial rate factors for phenylation of pyridine (Hey and Williams 1953) and the overall reactivity relative to benzene. It has been pointed out elsewhere (Brown 1953, 1956, further results in press) that the discussion of radical reactivities of heterocyclic systems in terms of free valences cannot be justified except on an empirical basis. It is clear from Table 1 that the free valences disagree with the observed reactivities for either value of h because experimentally the 3- and 4-positions have virtually the same reactivity as a benzene position, whereas the free valence of the 4-position always indicates a much enhanced reactivity. The value for the 3-position is in agreement with the observed reactivity for $h=0{\cdot}5$ and it is interesting that the use of free valence as a criterion of reactivity can be justified for the 3-position of pyridine but not for the 2- or 4-position (Brown 1956, in press). The lack of agreement of free valences with experiment must therefore be attributed to their unjustified use as a criterion of reactivity rather than to a failure of the molecular-orbital theory of chemical reactivity.

In confirmation of the results of phenylation of pyridine, bromination of pyridine at 500 °C, which doubtless proceeds through homolytic attack of the heterocycle by bromine atoms, gives predominantly 2-bromopyridine (Wibaut and Nicolai 1939 ; Wibaut and den Hertog 1945).

Table 2 presents the theoretical results for pyrimidine (II). Both π-electron densities and localization energies predict the order of reactivities of the positions towards electrophilic reagents to be 5>4>2. Experimentally, no electrophilic substitutions have been observed for pyrimidine itself although a reactivity similar to that of benzene is predicted for the free base. The low reactivity is again to be ascribed to cation formation in acid media rather than to any π-electron effect. However, substituted-pyrimidines carrying activating groups

are susceptible to attack by electrophils, halogenation (English *et al.* 1946; Shepherd and Fellows 1948; Price, Leonard, and Whittle 1945), nitration (Hartman and Sheppard 1943), nitrosation (Traube 1904), and chloromethylation (Schmedes 1925), all occurring at the 5-position.

For nucleophilic attack both approximations agree in predicting the reverse order of reactivities, namely $2>4>5$. Experimentally the only observation which might have some relevance is that amination of 4-methylpyrimidine produces the 2,4-diamino-compound (Davies, Johnson, and Piggott 1945;

TABLE 2

THEORETICAL RESULTS FOR PYRIMIDINE POSITIONS

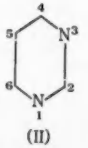
h	Position	A_e (—β)	A_r (—β)	A_n (—β)	q*	F†
0·5	2	2·8654	2·5382	2·2111	0·845	0·416
	4	2·6909	2·5272	2·3636	0·874	0·415
	5	2·5391	2·5391	2·5391	1·009	0·398
2·0	2	3·4557	2·4557	1·4557	0·467	0·610
	4	3·1456	2·3783	1·6110	0·632	0·562
	5	2·5788	2·5788	2·5788	1·029	0·380

* π-Electron density.

† Free valence (max. bond No. 1·732).

Davies and Piggott 1945). The reactivities of attached methyl groups should follow the same order as nucleophilic reactivities, as pointed out for pyridine, and it is known (Gabriel and Colman 1908; Brown and Ross 1948; Ross 1948) that aldehydes condense with methyl substituents in the 2- and 4-positions, but not in the 5-position.

For homolytic substitution the localization energies predict the order of reactivities of positions to be $4>2>5$. The free valences disagree with this order but it is only at the 5-position that one may justify using the free valence as



(II)

a measure of reactivity. No direct experimental evidence for radical attack is available but an attempt to couple diazotized *p*-nitraniline with pyrimidine gave small amounts of 2- and 4-(*p*-nitrophenyl)pyrimidine (Lythgoe and Rayner 1951). The present theoretical results enable us to account for these products by assuming that the diazonium salt decomposes to yield aryl radicals which attack the pyrimidine preferentially at the 2- and 4-positions.

In Table 3 the theoretical data for pyrazine (III) are summarized. On comparing the values for the charge densities and localization energies of pyrazine

with those of pyridine and pyrimidine it is seen that electrophilic and nucleophilic substitution should take place about as readily as in the α-position in pyridine, Radical attack is also predicted (from A_r) to occur more readily than in benzene. and it is interesting to observe that the reactivity of the conjugate acid is predicted to be much greater than that of free pyrazine, suggesting that it might be interesting to study homolytic substitution in an acidic medium.

TABLE 3

THEORETICAL RESULTS FOR PYRAZINE

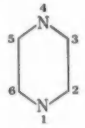
h	Position	A_e (—β)	A_r (—β)	A_n (—β)	q*	F†
0·5	2	2·6641	2·5008	2·3375	0·926	0·411
2·0	2	2·6675	2·1381	1·6088	0·735	0·557

* π-Electron density.

† Free valence (max. bond No. 1·732).

Experimentally, it has been found possible to chlorinate pyrazine in the vapour phase at relatively high temperatures (Sayward 1945). This reaction might conceivably proceed through radical attack by halogen atoms.

Although, theoretically, the amination reaction with sodium amide would be expected to occur about as readily as it does at the α-position in pyridine it has been found that the reaction with unsubstituted-pyrazine gives only very



(III)

small yields of aminopyrazine (Shreve and Berg 1947). This might constitute a partial failure of the molecular-orbital theory on a quantitative scale, but in view of the doubts expressed concerning the amination mechanism (Badger 1954) one must reserve judgment until the reaction mechanism is better understood.

The calculated π-electron densities do appear to reflect correctly the reactivity of pyrazine because methyl substituents, for example, in 2,5-dimethylpyrazine, condense with aromatic aldehydes (Francke 1905).

III. CONCLUSION

The preceding study of the molecular-orbital theory of chemical reactivity reinforces the conclusions drawn in a previous paper (Brown 1955). The theory at present provides a satisfactory interpretation of the chemistry of these heterocycles. However, on the experimental side the results are not always clear-cut and it is possible that more extensive quantitative experimental studies will reveal the limitations of the present theory.

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SYNTHETIC ANALGESICS: PIPERAZINE ANALOGUES OF 6–DIMETHYLAMINO–4,4–DIPHENYLHEPTAN–3–ONE (" METHADONE ")

By J. Cymerman-Craig,* R. J. Harrisson,* M. E. Tate,* R. H. Thorp,† and R. Ladd†

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Summary

4,4-Diphenyl-6-(4-methyl-1-piperazino)heptan-3-one (II ; R=Me) and 3,3-diphenyl-1-(4-methyl-1-piperazino)hexan-4-one (II ; R=H) have been prepared, the former showing analgesic activity approaching that of morphine, while the latter is inactive. Nevertheless, the methiodide (V) of the inactive base has activity approaching that of morphine. An explanation for these findings is advanced.

I. Introduction

Since the development of the potent morphine-like analgesic " methadone " (6-dimethylamino-4,4-diphenylheptan-3-one) (I ; $R^1=R^2=R^3=Me$) numerous analogues of this substance have been prepared (for reviews, see Small 1948 ; Eddy 1950). Variation in the nature of R^2 and R^3 in I usually results only in an alteration in biological side reactions without serious effect on analgesic activity. No substances of this type containing a piperazino-substituent as the basic group were known, and in view of the high activity of the morpholino-analogue (I ; $R^1=Me$, NR^2R^3=1-morpholino) (Attenburrow *et al.* 1949) it was of interest to examine 4,4-diphenyl-6-(4-methyl-1-piperazino)heptan-3-one (II ; R=Me), the piperazino-analogue of " methadone ".

The condensation of 3-bromo-1,1-diphenyl-*n*-butyl cyanide with morpholine was first investigated as a model for the condensation of this cyanide with 1-methylpiperazine. Reaction at 140 °C for 12 hr gave the desired 1,1-diphenyl-3-morpholino-*n*-butyl cyanide in 15 per cent. yield. Catalytic amounts of anhydrous potassium carbonate (5 per cent. yield) or copper powder (6 per cent. yield) inhibited the reaction, while copper sulphate afforded a 30 per cent. yield after 6 hr at 140 °C, not increased (24 per cent. yield) by extending the reaction period to 50 hr. Application of these results to the condensation with 1-methyl-piperazine gave 1,1-diphenyl-3-(4-methyl-1-piperazino)-*n*-butyl cyanide (III ; R=Me) in 24 per cent. yield. Absence of the copper sulphate catalyst, or extension of the reaction period to 48 hr, reduced the yield to 16 per cent. An alternative synthesis by condensation of piperazine with the above bromo-cyanide gave the oily 1,1-diphenyl-3-(1′-piperazino)-*n*-butyl cyanide in lower yield ; this on methylation afforded III (R=Me). Ethylmagnesium bromide

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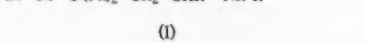
with III (R=Me) gave a ketimine readily hydrolysed to 4,4-diphenyl-6-(4-methyl-1-piperazino)heptan-3-one (II; R=Me).

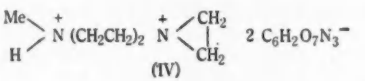
Removal of the methyl side-chain from methadone greatly reduces analgesic activity (Chen 1948), and the synthesis of II (R=H) was undertaken in order to examine whether a similar effect would occur.



(I)

(II)

(III)



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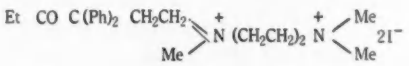

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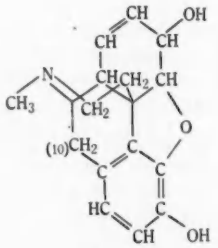

(VI)

Methylation of 1,2′-hydroxyethylpiperazine with formic acid and formaldehyde gave 1,2′-hydroxyethyl-4-methylpiperazine as a crystalline solid; it had previously been reported as an oil (Wright, Kolloff, and Hunter 1948). Methylation using zinc dust, formaldehyde, and hydrochloric acid gave a lower yield.

Chlorination afforded the unstable 1,2′-chloroethyl-4-methylpiperazine, characterized as the dipicrate. This lost hydrogen chloride, presumably forming 1-ethyleneiminium-4-methylpiperazinium dipicrate (IV), and the latter on further crystallization was changed to a high-melting insoluble substance, probably a dimeric piperazinium salt analogous to those described by Schultz,

Robb, and Sprague (1947) (cf. Knorr 1904 ; Golumbic, Fruton, and Bergmann 1946).

Condensation of 1,2′-chloroethyl-4-methylpiperazine with sodiodiphenylmethyl cyanide gave 1,1-diphenyl-3-(4-methyl-1-piperazino)-*n*-propyl cyanide. Ethylmagnesium bromide furnished the stable ketimine, 3,3-diphenyl-4-imino-1-(4-methyl-1-piperazino)-*n*-hexane, resistant to hydrolysis with both dilute (2N) and concentrated (10N) hydrochloric acid, but hydrolysed by hydrobromic acid to 3,3-diphenyl-1-(4-methyl-1-piperazino)hexan-4-one (II ; R=H). The base and many of its salts were hygroscopic, but the diacid oxalate and dimethiodide (V) were stable. Preliminary pharmacological examination comprised the determination of toxicity by intravenous injection in mice, and analgesic tests in comparison with morphine by the method of Thorp (1946), made with doses of half the LD_{50} given subcutaneously in rats. The results are shown in Table 1, from which it is seen that the methadone-analogue (II ;

TABLE 1

ANALGESIC ACTIVITIES

Groups of 10 rats were used in each experiment

Compound	LD_{50} (mg/kg)	Dose Level (mg/kg)	Activity
Morphine..	—	5	1·0
4,4-Diphenyl-6-(4-methyl-1-piperazino)heptan-3-one (II ; R=Me)	16	8	0·5–0·7
3,3-Diphenyl-1-(4-methyl-1-piperazino)hexan-4-one (II ; R=H) as diacid oxalate ..	80	40	⩽0·1
3 , 3 - Diphenyl - 1 - (1′, 4′, 4′ - trimethyl - 1′ - piperazinium)hexan-4-one dimethiodide (V)	15	8	0·5–0·7
6 - Dimethylamino - 4,4 - diphenylheptan - 3 - one (" methadone ") (I ; $R^1=R^2=R^3$=Me) ..	—	—	1·3*

* Walton, Ofner, and Thorp (1949).

R=Me) showed analgesic activity approaching that of morphine, while the demethyl compound (II ; R=H) was almost devoid of activity. However, the dimethiodide (V) of the latter had activity equal to that of II (R=Me) again approaching that of morphine.

It is known that quaternization of the basic group in methadone itself markedly decreases analgesic activity (Eddy, Touchberry, and Lieberman 1950 ; Jensen, Lauridsen, and Christensen 1948). However, inspection of molecular scale models (Catalin Ltd.) of morphine (VI) II (R=Me), II (R=H), and V, shows (i) that the side-chain methyl group R^1 in I and R in II simulates the carbon atom C_{10} in morphine ; and (ii) that the change of configuration of the nitrogen atom from the pyramidal structure in II (R=H) to the tetrahedral structure

in V results in a re-orientation of the nitrogen valencies by which the quaternary methyl group at N_1 now simulates the side-chain methyl group R in II. This would explain the activity of V and the inactivity of II (R=H). Further investigations are in progress.

II. Experimental

Analyses are by Miss B. Stevenson, University of Sydney, and Dr. K. W. Zimmermann, C.S.I.R.O. Microanalytical Laboratory.

(*a*) *1,2′-Hydroxyethyl-4-methylpiperazine.*—1,2′-Hydroxyethylpiperazine (7·2 g ; 0·055 mol) was added gradually with ice-cooling to 90% formic acid (5·8 g ; 0·125 mol) and 36% aqueous formaldehyde (4·6 g ; 0·055 mol) then added slowly. The temperature was raised until effervescence commenced and the mixture kept on the steam-bath until effervescence ceased (6 hr). Concentrated HCl (11 ml) was added and the excess formic acid and formaldehyde were removed by distillation. The residue was made strongly alkaline with 50% NaOH solution and the oily base extracted with chloroform. Distillation of the dried (Na_2SO_4) extract gave 6·0 g (75% yield) of 1,2′-hydroxyethyl-4-methylpiperazine as a colourless oil, b.p. 88 °C/3 mm, 109–110 °C/10 mm, n_D^{24} 1·4848 (Wright, Kolloff, and Hunter (1948) give b.p. 73–75 °C/3 mm). On standing the oil solidified to plates, m.p. 37·5–38 °C (Found : N, 19·6%. Calc. for $C_7H_{16}ON_2$: N, 19·5%).

(*b*) *1,2′-Chloroethyl-4-methylpiperazine.*—An ice-cold solution of 1,2′-hydroxyethyl-4-methylpiperazine (2·3 g ; 0·016 mol) in dry benzene (20 ml) was treated gradually with thionyl chloride (3·8 g ; 0·032 mol). The mixture was refluxed for 30 min, the solid hygroscopic dihydrochloride filtered off, washed with ether, and dissolved in NaOH solution. The base was extracted with benzene and the benzene solution dried azeotropically by concentrating *in vacuo* to 50 ml. For synthetic work the product should be used immediately.

A sample of the dihydrochloride was dissolved in water and converted to the *dipicrate* which crystallized from 2-ethoxyethanol in needles, m.p. 235–236 °C (decomp.) (Found : C, 36·6 ; H, 3·6 ; N, 17·5%. Calc. for $C_7H_{15}N_2Cl.2C_6H_3O_7N_3$: C, 36·8 ; H, 3·4 ; N, 18·0%). After two recrystallizations from 2-ethoxyethanol this showed m.p. 242·5–243 °C and was presumably *1-ethyleneiminium-4-methylpiperazinium dipicrate* (*IV*) (Found : C, 38·8 ; H, 4·0%. Calc. for $C_{19}H_{20}O_{14}N_8$: C, 39·1 ; H, 3·6%). Repeated recrystallization from 2-ethoxy- or 2-methoxyethanol sharply raised the m.p. to give yellow microcrystals, m.p. >360 °C (Found : C, 38·9 ; H, 3·9%), presumably the *dimeric dipicrate.*

(*c*) *1,1-Diphenyl-3-(4-methyl-1-piperazino)-n-propyl Cyanide* (*III ; R=H*).—Freshly crushed sodamide (10 g ; 0·25 mol) was quickly added to a solution of diphenylmethyl cyanide (40 g ; 0·2 mol) in dry benzene (150 ml) ; the solution darkened immediately and after refluxing for 1 hr was black. A solution of 1,2′-chloroethyl-4-methylpiperazine (from 0·1 mol of 1,2′-hydroxyethyl-4-methylpiperazine as described above) in benzene (50 ml) was added to the cooled and stirred solution and the reaction mixture was stirred at 25 °C for 14 hr during which time it became light brown in colour. It was then extracted several times with HCl (2N) and the extracts basified with 50% NaOH solution and extracted with chloroform. Removal of solvent from the dried extracts left an oil which solidified on trituration with light petroleum (b.p. 40–70 °C) from which it crystallized (20 g, 61% yield calc. on 1,2′-hydroxyethyl-4-methylpiperazine) in rhombs, m.p. 99·5–100 °C, of *1,1-diphenyl-3-(4-methyl-1-piperazino)-n-propyl cyanide* (Found : C, 78·8 ; H, 7·9 ; N, 12·9%. Calc. for $C_{21}H_{25}N_3$: C, 78·9 ; H, 7·9 ; N, 13·1%). The *dipicrate* crystallized from 2-ethoxyethanol in needles, m.p. 250 °C (Found : N, 15·9%. Calc. for $C_{21}H_{25}N_3.2C_6H_3O_7N_3$: N, 16·2%).

The following conditions for the preparation of this cyanide were investigated : After addition of chloroamine, the reaction mixture was (i) refluxed 3 hr, then stirred 3 hr at 20 °C : 18% yield ; (ii) stirred 6 hr at 20 °C : 27% yield ; (iii) stirred 12 hr at 20 °C : 46% yield ; (iv) stirred 15 hr at 16 °C : 60% yield.

(*d*) *3,3-Diphenyl-4-imino-1-(4-methyl-1-piperazino)-n-hexane.*—A solution of 1,1-diphenyl-3-(4-methyl-1-piperazino)-*n*-propyl cyanide (9·6 g ; 0·03 mol) in dry toluene (50 ml) was added

to a solution of ethylmagnesium bromide (from 2·4 g of magnesium) in ether (100 ml) and the temperature raised to 95 °C by distilling off the ether. The mixture was then stirred at 95 °C for a further 16 hr, cooled, and the complex decomposed by addition of HCl (100 ml ; 2N). The toluene layer was washed with dilute HCl, the combined acid portions made alkaline with 50% NaOH, and the magnesium hydroxide removed by centrifuging. The aqueous layer and the magnesium hydroxide were extracted with chloroform and the dried (Na_2SO_4) chloroform extracts on distillation gave the imine (8 g, 76% yield) as an oil, b.p. 156–160 °C/0·06 mm, which did not solidify. It gave a *dipicrate* crystallizing from 2-ethoxyethanol as microcrystalline prisms, m.p. 231 °C (decomp.) (Found : C, 51·9 ; H, 4·3 ; N, 15·1%. Calc. for $C_{23}H_{29}N_3.2C_6H_3O_7N_3$: C, 52·0 ; H, 4·6 ; N, 15·6%). The imine was unchanged after refluxing with HCl (2N) for 2 hr.

(*e*) *3,3-Diphenyl-1-(4-methyl-1-piperazino)hexan-4-one* (*II ; R=H*).—The above imine (7 g) was refluxed with HBr (50 ml ; 20%) for 8·5 hr. The cooled solution was basified with 40% sodium hydroxide solution and extracted with chloroform. Removal of solvent gave *3,3-diphenyl-1-(4-methyl-1-piperazino)hexan-4-one* (3·8 g, 55% yield) as a pale yellow viscous oil, b.p. 151–165 °C/0·05 mm, n_D^{15} 1·5716 (Found : N, 8·4%. Calc. for $C_{23}H_{30}ON_2$: N, 8·1%). The *dipicrate* formed needles from 2-ethoxyethanol, m.p. 238·5 °C (Found : C, 52·4 ; H, 4·7 ; N, 13·9%. Calc. for $C_{23}H_{30}ON_2.2C_6H_3O_7N_3$: C, 52·0 ; H, 4·5 ; N, 13·8%), and the *diacid oxalate*, prepared from the base and anhydrous ethanolic oxalic acid, had m.p. 219 °C (Found : N, 5·4%. Calc. for $C_{23}H_{30}ON_2.2C_2H_2O_4$: N, 5·3%).

Treatment of the base with methyl iodide gave *3,3-diphenyl*-1-(*1',4',4'-trimethyl*-1'-*piperazinium*)*hexan-4-one di-iodide*, crystallizing from methanol-ethanol as yellowish rhombs, m.p. 266–267 °C (decomp.) (Found : N, 4·7 ; O, 3·2 ; I, 40·7 ; N-Me, 14·5%. Calc. for $C_{25}H_{36}ON_2I_2$: N, 4·5 ; O, 2·7 ; I, 40·0 ; 3N-Me, 13·8%).

Treatment of the dimethiodide with aqueous lithium picrate gave *3,3-diphenyl-1-(1',4',4'-trimethyl-1'-piperazinium)hexan-4-one dipicrate*, crystallizing from acetone-ether as yellow needles, m.p. 201 °C (Found : N, 13·4%. Calc. for $C_{37}H_{40}O_{15}N_8$: N, 13·4%).

(*f*) *1,1-Diphenyl-3-(4-methyl-1-piperazino)*-n-*butyl Cyanide* (*III ; R=Me*).—A mixture of 1-methylpiperazine (16·4 g ; 0·16 mol), 3-bromo-1,1-diphenyl-*n*-butyl cyanide (26 g ; 0·08 mol) (Easton, Gardner, and Stevens 1947) and anhydrous copper sulphate (0·1 g) was refluxed for 6 hr at 170 °C. During this time the reaction mixture separated into an upper (pale yellow) and a lower (dark brown) layer. The cooled reaction mixture was treated with ether and extracted with HCl (2N). The aqueous acidic extracts were basified at 0 °C and the liberated base extracted into chloroform. Removal of solvent afforded the *cyanide* as an oil (6·6 g, 24% yield) which crystallized on standing. From light petroleum (b.p. 60–90 °C) it formed white needles, m.p. 107 °C (Found : C, 79·3 ; H, 8·5%. Calc. for $C_{22}H_{27}N_3$: C, 79·2 ; H, 8·2%). The *dipicrate* crystallized from acetone as solvated needles, m.p. 229 °C (Found : N, 15·1%. Calc. for $C_{22}H_{27}N_3.2C_6H_3O_7N_3.C_3H_6O$: N, 14·9%).

(*g*) *1,1-Diphenyl-3-(1'-piperazino)*-n-*butyl Cyanide*.—Reaction of anhydrous piperazine (11·5 g ; 0·13 mol), 3-bromo-1,1-diphenyl-*n*-butyl cyanide (14·0 g ; 0·045 mol), and anhydrous copper sulphate (0·5 g) as described in (*f*) gave a basic product (5·8 g) the petroleum-soluble portion of which was an oil and gave *1,1-diphenyl-3-(1'-piperazino)*-n-*butyl cyanide dipicrate*, crystallizing from acetone as solvated yellow needles, m.p. 184 °C (Found : N, 14·8 ; O, 28·5%. Calc. for $C_{21}H_{25}N_3.2C_6H_3O_7N_3.C_3H_6O$: N, 15·1 ; O, 28·7%).

Methylation of the petroleum-soluble oily cyanide by refluxing for 6 hr with formic acid and formaldehyde at 100 °C and working-up as described in (*a*) gave 1,1-diphenyl-3-(4-methyl-1-piperazino)-*n*-butyl cyanide, m.p. 106–107 °C, undepressed on admixture with the material prepared in (*f*). It gave a dipicrate, m.p. and mixed m.p. 229 °C.

(*h*) *4,4-Diphenyl-6-(4-methyl-1-piperazino)heptan-3-one* (*II ; R=Me*).—Reaction of 1,1-diphenyl-3-(4-methyl-1-piperazino)-*n*-butyl cyanide (1·96 g ; 0·006 mol) with ethylmagnesium bromide (from 0·57 g of magnesium) was carried out exactly as described in (*d*). The combined acid extracts were refluxed with HCl (2N) for 2·5 hr to hydrolyse the imine, and then basified and extracted with chloroform. Removal of solvent gave a solid residue (1·96 g) crystallizing

from aqueous methanol as prisms, m.p. 118–118·5 °C, of *4,4-diphenyl-6-(4-methyl-1-piperazino)-heptan-3-one* (Found : C, 78·6 ; H, 8·5 ; N, 8·2 ; O, 4·5%. Calc. for $C_{24}H_{32}ON_2$: C, 79·0 ; H, 8·8 ; N, 7·7 ; O, 4·4%). The substance could be sublimed at 110 °C/0·01 mm. The *dipicrate* formed needles from acetone, m.p. 203 °C (Found : N, 13·7 ; O, 29·3%. Calc. for $C_{24}H_{32}ON_2.2C_6H_3O_7N_3$: N, 13·6 ; O, 29·2%).

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STUDIES IN RELATION TO BIOSYNTHESIS

VIII. TASMANONE, DEHYDROANGUSTIONE, AND CALYTHRONE

By A. J. Birch* and Patricia Elliott*

[*Manuscript received September 2, 1955*]

Summary

Tasmanone from the oil of *Eucalyptus risdoni* Hook. gives a crystalline copper salt and imine and by acid hydrolysis produces 1,1,3-trimethylphloroglucinol. Its probable constitution is discussed.

Evidence is presented for assigning to dehydroangustione the formula III and to calythrone the formula IX. The biogenetic relations of these substances are discussed.

I. Tasmanone

It has been pointed out (Birch 1951) that a number of compounds from Australian essential oils are β-triketones containing the group $HC(-C=O)_3$ which confers "phenolic" properties. The compounds form ether-soluble copper salts and give red colours with ferric chloride. A summary (Elliott 1953) has shown that about eight out of 10 of the leaf oils of the Australian families Myrtaceae and Rutaceae are reported to contain phenolic fractions ranging up to 2 per cent., characterized by giving red or brown colours with ferric chloride. These may well be mixtures of β-triketones, the related acylphenols, or salicylaldehyde derivatives (cf. Birch and Elliott 1953; Birch, Elliott, and Penfold 1954). The oils from *Melaleuca acuminata* F. Muell. and *Eucalyptus macarthuri* Deane & Maiden, chosen merely because they were available, contained a small proportion of phenolic compounds which gave ether-soluble blue copper salts as non-crystallizable oils. They therefore contain compounds with chelating structures. The oil of *E. polybractea* Baker was found to contain some "macropone" (4-*iso*propylsalicylaldehyde) (Birch and Elliott 1953) together with other chelating compounds.

The best characterized of such "phenols" not already investigated closely is tasmanol (Robinson and Smith 1915; Baker and Smith 1920) which is reported to occur in the oils of the Tasmanian trees *E. risdoni* Hook. and *E. linearis* Cunn. It was investigated by Trikojus and White (1932) who assigned to it a possible formula $C_{13}H_{22}O_3$ and considered it to be an acid because of its solubility in carbonate solution, and because it formed a crystalline *p*-toluidide and a neutral methyl ester hydrolysed by alkali.

In the University Collection there was available about a litre of oil labelled "*Eucalyptus risdoni*, crude oil" which had been isolated by the late H. G.

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Smith about 1920. Extraction with alkali gave 0·2 per cent. of a "phenolic" fraction of which about 75 per cent. was soluble in carbonate but not in bicarbonate and represented crude tasmanol. The action of cupric acetate in methanol gave an ether-soluble copper salt, m.p. 114 °C, which had an analysis approximating to $(C_{14}H_{19}O_4)_2Cu$. The substance obtained by the action of hydrochloric acid was a pale yellow oil which showed ketonic properties by giving a derivative with 2,4-dinitrophenylhydrazine. The same copper salt, m.p. 112 °C, was also obtained from a small specimen of Smith's labelled "tasmanol". The substance recovered after refluxing with 2N sodium hydroxide solution still gave a red ferric reaction and is therefore unlikely to be a β-diketone; the β-triketones with three carbonyl groups attached to the same carbon atom are stable to mild alkaline hydrolysis. The ultraviolet absorption spectrum ($\lambda_{max.}$ 245 mμ, log $\varepsilon_{max.}$ 4·09; $\lambda_{max.}$ 273 mμ, log $\varepsilon_{max.}$ 3·81; $\lambda_{max.}$ 325 mμ, log $\varepsilon_{max.}$ 3·90) is similar to that of 1,1,3-trimethyl-5-acetylphloroglucinol (I) (Reidl and Risse 1954) ($\lambda_{max.}$ 230 mμ, log $\varepsilon_{max.}$ 4·1; $\lambda_{max.}$ 280 mμ, log $\varepsilon_{max.}$ 3·95; $\lambda_{max.}$ 280 mμ, log $\varepsilon_{max.}$ 3·7; $\lambda_{max.}$ 333 mμ, log $\varepsilon_{max.}$ 4·0).

The purification of dehydroangustione (see below) was facilitated by its ability to form a crystalline imine (Gibson, Penfold, and Simonsen 1930). The "tasmanol", now renamed tasmanone because of its ketonic nature (compare the analogous leptospermone) gave rise to an imine, m.p. 90 °C, $C_{13}H_{19}O_3N$, which was less useful for purification because of its low m.p. and high solubility. The "*p*-toluidide" of Trikojus and White (1932) is probably the *p*-tolylimine. Their "ester" is probably an enol-ether.

Hydrolysis of tasmanone with 10N hydrochloric acid gave a volatile fraction, shown by paper chromatography to contain acetic acid and a butyric, probably *iso*butyric acid, and a trace of what may be a valeric acid, but which is neither *n*-valeric nor *iso*valeric acid. The non-volatile portion contained 1,1,3-trimethylphloroglucinol, m.p. 177 °C, undepressed by an authentic specimen m.p. 178 °C. A less pure fraction was also obtained with m.p. 167 °C undepressed by 1,1,3-trimethylphloroglucinol, and it is possible that other methylated phloroglucinol derivatives, for example, 1,1-dimethylphloroglucinol, may be present. The ultraviolet absorption ($\lambda_{max.}$ 246 mμ, log $\varepsilon_{max.}$ 3·93; $\lambda_{max.}$ 280 mμ, log $\varepsilon_{max.}$ 3·84) of the fraction, m.p. 167 °C is similar to that of 1,1-dimethylphloroglucinol ($\lambda_{max.}$ 244 mμ, log $\varepsilon_{max.}$ 4·18; $\lambda_{max.}$ 283 mμ, log $\varepsilon_{max.}$ 3·4) (Birch and Todd 1952); an extra methyl group would not be expected to cause any very marked change in the position of the maxima.

In endeavours to obtain more tasmanone to complete the structure determination, five batches of leaves from *E. risdoni* and two from closely related species *E. tasmanica* Blakely and the hybrid *E. tasmanica* × *E. salicifolia* (Sol.) (Cav.) were obtained at different times of the year and from different sources near Hobart, through the kindness of Dr. I. R. C. Bick and Professor H. N. Barber. In several cases traces of crystalline copper salts were obtained. In one case this had m.p. 92–93 °C (the first specimen above had m.p. 114 °C) and the m.p. could not be raised. The recovered triketone did not produce any crystalline imine. The analysis of the salt was slightly different and corresponded approximately to an equimolecular mixture of $(C_{14}H_{19}O_4)_2Cu$ and $(C_{13}H_{17}O_4)_2Cu$. Two

methoxyl groups were present for each copper atom. None of the original salt, m.p. 114 °C, remained for a methoxyl analysis. In another case a small amount of copper salt, m.p. 97 °C, analysed approximately for $(C_{14}H_{19}O_4)_2Cu$.

On the basis of the above results we suggest that " tasmanol " is probably a mixture of II (R=H) and II (R=Me) (tasmanone) which was probably the major constituent of the original specimen. There is at any rate clear evidence of the presence of a derivative of 5-acyl-1,1,3-trimethylphloroglucinol, thus completing the series of natural acyl phloroglucinols of all degrees of methylation from 0 to 4. The nature of the ketonic side-chain is still uncertain; the *iso*-butyric acid noted above could conceivably have been produced by breakdown of the ring, and other side-chains may be present in small proportion. The analogues of lupulone and humulone provide good examples of the occurrence of such mixtures (e.g. Howard and Tatchell 1954).

A sample of *E. linearis* obtained through the kindness of Mr. A. R. Penfold contained no tasmanone. Until botanical investigation can reveal the source of the original " tasmanol " further structural work is necessarily in abeyance.

II. Structure of Dehydroangustione

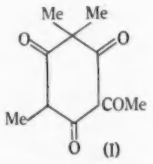
On the basis chiefly of published evidence formula IV* was advanced as a probable one for dehydroangustione (Birch 1951). The purely chemical evidence would have favoured III* but the infra-red absorption spectrum appeared to indicate the presence of $C{=}CH_2$. However, the biogenetic considerations discussed below strongly favour III and the problem has been accordingly reinvestigated.

An outstanding difficulty to the acceptance of either III or IV is that dehydroangustione has been described as optically active (Cahn *et al.* 1931). As has already been pointed out (Birch 1951) this may be due to the presence of its dihydro-derivative angustione as an impurity. We have now obtained dehydroangustione imine in a state of purity as shown by its elevated m.p. (157·5 °C compared with 152 °C) and by the absence of characteristic peaks in the infra-red due to angustione imine, and it is in fact optically inactive, as is the dehydroangustione recovered from it.

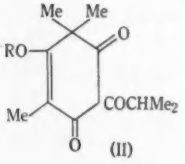
Two outstanding pieces of evidence in favour of formula I are the production of dimethylmalonic acid by permanganate oxidation and the formation by acid hydrolysis of the trimethyl*cyclo*hexenone (V) (Gibson, Penfold, and Simonsen 1930; Cahn *et al.* 1931). We have repeated the oxidation and have been unable to detect any of the 2,2-dimethylsuccinic acid to be expected from IV. The formation of V from IV would be explicable on the basis of double-bond shift under the vigorous conditions of hydrolysis, but this possibility was ruled out by showing that V can be reconverted to dehydroangustione by treatment with acetic anhydride and sodium acetate (for the method see Dieckmann and Stein 1904). A further proof of the correctness of I is afforded by the identical *C*-methyl analyses of dehydroangustione imine and angustione imine (2·1;

* These substances must be enols, but the direction of enolization is not clear and formulae are accordingly written in keto-forms (cf., however, Smith 1953).

theoretical 3). Ozonolysis of dehydroangustione or the imine failed to yield formaldehyde.* The infra-red spectra of the two imines were compared. They both contain a pronounced peak at 6·17μ and dehydroangustione imine has a strong peak at 11·37μ. It is evident that neither of these peaks can be due to the presence of $C{=}CH_2$. Dehydroangustione itself was re-examined through the kindness of Dr. C. L. Teitelbaum (Batelle Memorial Institute) and shows a peak at 11·3μ. This could be taken as strong evidence for the presence of $C{=}CH_2$ if it were not for the chemical evidence above (cf. Birch 1951). We are informed by Dr. G. D. Mealkins that conjugation may produce a band in this region and he considers that the evidence in fact favours formula III. The ultraviolet spectra of dehydroangustione ($\lambda_{max.}$ 230 and 283 mμ) and angustione ($\lambda_{max.}$ 243 and 276 mμ) are similar to known β-triketones (cf. Birch 1951).



(I)



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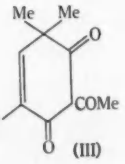

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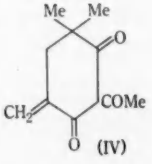

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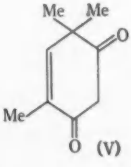


(V)

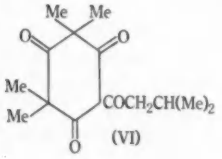
III. Biogenetic Relations of Tasmanone and Dehydroangustione

In Part IV of this series (Birch, Elliott, and Penfold 1954) it was pointed out that the structures of natural substances containing acylphloroglucinol nuclei could be explained by the hypothesis of biosynthesis from acetic acid units (Birch and Donovan 1953). An extension of the hypothesis requires that extra methyl and *iso*pentyl groups attached to the ring must have been introduced subsequent to the synthesis of the main skeleton (Birch, Elliott, and Penfold 1954). In order to be a probable process from the point of view of reaction mechanisms, the alkylation should take place on a carbon flanked by two intact carbonyl groups in the intermediate β-polyketo-acid or into the acylphloroglucinol ring. Substances such as III lacking a ring oxygen show strong structural affinities to phloroglucinol derivatives such as leptospermone (VI), butanofilicinic acid (VII), and tasmanone (II).

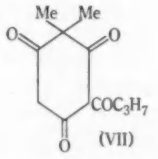
* Since this work was completed we have been informed by Professor C. H. Hassall that he and W. R. Chan (1955) have obtained a small yield of formaldehyde. They, however, do not regard IV as a probable formula.

Dehydroangustione (III) could clearly arise by this route (see below) if an appropriate carbonyl group in the intermediate methylated β-triketo-acid were reduced to an hydroxyl. Cyclization would then be accompanied by dehydration. An alternative but less likely explanation is that the incompletely aromatic 5-acetyl-1,1,3-trimethylphloroglucinol (I) is formed by methylation before or after ring closure and the 2-keto-group is then reduced. Attempts to reduce this compound or its anil with sodium borohydride were unsuccessful. It is clear that an origin of the above type would readily lead to a double bond in the position found in III, but not in IV, and it was chiefly on these grounds that the latter formula was originally questioned.

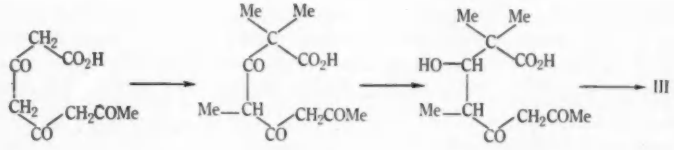
It may be significant that the oil of *Backhousia angustifolia* Benth. contains not only dehydroangustione and angustione but also angustifolionol (5-hydroxy-7-methoxy-2,6,8-trimethylchromone) which, though superficially considerably different in structural type, can also be hypothetically constructed from acetic acid units accompanied by methylation (Birch, Elliott, and Penfold 1954).

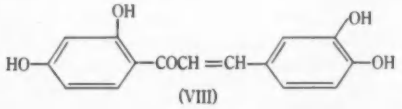


(VI)



(VII)





(VIII)

The problem of removal of oxygen during biosynthesis from phenolic and enolic systems of the type considered above is of considerable general importance. For example, the production of butein (VIII) in *Dahlia variabilis* is controlled by a gene, in the presence of which this resorcinol derivative is preponderantly formed instead of phloroglucinol derivatives such as apigenin. The picture here is complicated by varying degrees of hydroxylation of the other benzene ring, and the problem will be discussed in detail at a later stage. It appears to us, however, that the reduction of a carbonyl group in an intermediate (cf. Birch and Donovan 1953) is an acceptable alternative to the scheme which requires reductive removal of an hydroxyl from an aromatic ring. Jain, Gupta,

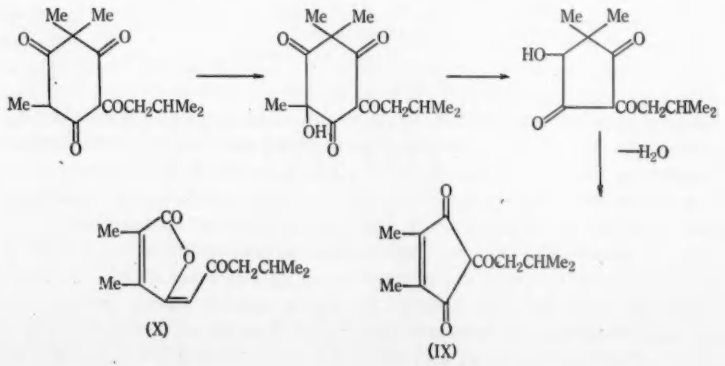
and Seshadri (1953), Jain, Mittal, and Seshadri (1953), and Jain and Seshadri (1953*a*, 1953*b*, 1953*c*), have succeeded in carrying out such reductions using the aryl toluenesulphonate and Raney nickel, but from a mechanistic viewpoint this kind of reaction is unlikely to be a valid analogy to a biochemical process. The reduction of a carbonyl group, for example, in acetoacetic acid, is a well-known biochemical process.

IV. Structure of Calythrone

Calythrone, from the oil of *Calythrix tetragona* Lab., was formulated as IX (Birch 1951) rather than X (Penfold and Simonsen 1940), on the basis of published evidence and of a comparison of properties with synthetic 2-*iso*valeryl indane-1,3-dione. Through the kindness of Mr. A. R. Penfold we have now examined the ultraviolet and infra-red spectra of calythrone, which favour IX. It shows maximal absorption at $\lambda_{max.}$ 240 mμ, log ε 4·29 and $\lambda_{max.}$ 266 mμ, log ε 4·26 (ethanol). The chromophore of X would undoubtedly absorb at a wavelength longer than 300 mμ, although no exact analogies are known to us. The infra-red spectrum has a series of strong bands in the region 6–8μ as with other β-triketones (Birch 1951) and there is no indication of the lactone band below 5·6μ (probably 5·3–5·6μ, Woodward and Kovach 1950) required for X. Reduction of calythrone by means of sodium amalgam, followed by steam distillation resulted in the formation of *iso*valeraldehyde, to be expected from IX (cf. Birch and Todd 1952). Formula X would not however be completely excluded by this result.

V. Biogenetic Relations of Calythrone

Calythrone is the only known exception to the occurrence of six-membered rings in β-triketones as demanded by the acetate hypothesis (cf. Section II). The ready formation of a five-membered from a six-membered ring is already known in the humulone series (Wieland and Martz 1926 ; Harris, Howard, and Pollock 1952), and by analogy with this and with an additional dehydration stage involving a Wagner-Meerwein rearrangement, the following biogenetic scheme is a plausible one :



VI. Experimental

(*a*) *Tasmanone.*—(i) *Extraction.* Oil labelled "*Eucalyptus risdoni*, crude oil" (500 c.c.) was shaken with three successive portions (20 c.c.) of aqueous sodium hydroxide (5%); some emulsification occurred. The aqueous solution was extracted with ether (30 c.c.) and acidified. The oil ("tasmanol") was taken up in ether (50 c.c.) and extracted successively with saturated sodium bicarbonate solution (50 c.c.) (extract *A*); aqueous sodium carbonate (5%; 4×40 c.c.) (extract *B*); and finally, with aqueous sodium hydroxide (5%; 20 c.c.) (extract *C*). Acidification gave: extract *A* a small amount of oil smelling of lower fatty acid; extract *B* crude tasmanone (0·9 g); and extract *C* a small amount of oil with a phenolic odour which did not give a copper salt. The crude tasmanone was refluxed for 30 min in methanol (5 c.c.) with finely powdered cupric acetate (1 g) and then poured into water. Ether extraction gave a deep blue solution which on evaporation left a blue gum. This was taken up in methanol (3 c.c.) and a few drops of water added to incipient turbidity. After several days the *copper salt* of tasmanone had crystallized and was recrystallized in the same manner to form bright blue prisms (0·5 g), m.p. 114 °C (Found: C, 59·2; H, 7·2%. Calc. for $C_{28}H_{38}O_8Cu$: C, 59·4; H, 6·7%). Tasmanone was regenerated from the salt by shaking with ether and 2N hydrochloric acid as a pale yellow oil with a characteristic odour; $\lambda_{max.}$ 245 mμ, log $\varepsilon_{max.}$ 4·09; $\lambda_{max.}$ 273 mμ, log $\varepsilon_{max.}$ 3·81; $\lambda_{max.}$ 325 mμ, log $\varepsilon_{max.}$ 3·9. Reaction with Brady's reagent gave a derivative, m.p. 222–224 °C from methanol.

(ii) *Tasmanone Imine.* Tasmanone (100 mg) from the copper salt, m.p. 114 °C dissolved in aqueous ammonia (2 c.c.) deposited a gum over 2 days which eventually crystallized. Recrystallized from light petroleum (b.p. 40–70 °C) *tasmanone imine* formed colourless needles, m.p. 90 °C (Found: C, 65·9; H, 8·7; N, 5·7%. Calc. for $C_{14}H_{21}O_2N$: C, 66·9; H, 8·4; N, 5·6%. Calc. for $C_{13}H_{19}O_2N$: C, 65·8; H, 8·0; N, 5·9%).

(iii) *Hydrolysis of Tasmanone.* Tasmanone (from the copper salt, 400 mg) was refluxed for 1 hr with 10N hydrochloric acid (15 c.c.). Water (25 c.c.) was then added and the solution distilled to remove about 15 c.c. of distillate. This distillate was neutralized with sodium hydroxide and evaporated to dryness, the residue acidified with dilute sulphuric acid and extracted with ether. After evaporation of the ether the residual oil was chromatographed on paper (by Mr. B. V. Chandler) by the method of Lindqvist and Storgards (1953). The ethylamine salts of the acids were run on Whatman No. 1 paper against the salts of acetic (R_F 0·19), propionic (R_F 0·29), *iso*butyric (R_F 0·43), butyric (R_F 0·46), and valeric (R_F 0·62) acids. The unknown acids gave three spots: R_F 0·19 (acetic); R_F 0·44 (butyric or *iso*butyric); R_F 0·58 (a valeric acid ?). The last spot was faint compared with the other two. In order to distinguish butyric from *iso*butyric acid, the solvent was allowed to run off the paper and the distance travelled by the spots referred to a standard acetic acid spot (R_a value): propionic 1·53; *iso*butyric 2·12; butyric 2·26; *iso*valeric 2·80; valeric 3·00. The unknown acids had R_a 1·00 (acetic), 2·08 (*iso*butyric), and 2·68 (neither valeric nor *iso*valeric acids).

The residual acid solution from the above distillation was filtered through sintered glass to remove a small amount of resin and the solution extracted with chloroform (4×10 c.c.). Evaporation of the chloroform gave a few mg of solid which was crystallized from water: methanol (2 : 1) to give cream coloured needles, m.p. 177 °C. There was insufficient for analysis, but the m.p. was not depressed by an authentic specimen of 1,1,3-trimethylphloroglucinol, m.p. 178 °C (Riedl and Risse 1954). The aqueous solution was evaporated under reduced pressure to 4 c.c., and on leaving a crystalline precipitate appeared. This was crystallized from water: methanol (2 : 1) to form cream coloured needles, m.p. 167 °C; a further crystallization failed to raise the m.p., but this was raised by admixture with the material m.p. 177 °C from the chloroform extraction. It is probably incompletely pure methylfilicinic acid (1,1,3-trimethylphloroglucinol) (Found: C, 63·5; H, 7·0%. Calc. for $C_9H_{12}O_3$: C, 64·3; H, 7·1%. Calc. for $C_8H_{10}O_3$: C, 62·3; H, 6·5%) $\lambda_{max.}$ 246 mμ, log $\varepsilon_{max.}$ 3·93; $\lambda_{max.}$ 280 mμ, log $\varepsilon_{max.}$ 3·84.

(iv) *Further Attempts to Isolate Tasmanone.* Samples of about 100 lb of leave and terminal branchlets of the following trees were distilled in steam at the Museum of Applied Arts and Sciences (Sydney) through the kindness of Mr. A. R. Penfold, and the oils extracted with aqueous sodium hydroxide.

E. tasmanica and a hybrid of *E. tasmanica* × *E. salicifolia* gave 100–200 mg of alkali-soluble material which gave only a trace of colour with ferric chloride and which appeared to consist chiefly of long-chain fatty acids.

E. linearis gave only a trace of alkali-soluble material.

E. risdoni. From sample 1 (21.xi.52) a small amount of copper salt, m.p. 104 °C, was obtained, insufficient for further examination.

Sample 2 (18.viii.53) contained no tasmanone whatever.

Sample 3 (21.xi.53). About 250 mg of alkali-soluble material gave a small quantity of copper salt, m.p. 97 °C (Found: C, 59·1; H, 7·1; residue, 13·7%. Calc. for $C_{28}H_{38}O_8Cu$: C, 59·5; H, 6·7; residue (CuO), 14·0%). No crystalline imine could be obtained.

Sample 4 (1.iii.54) contained alkali-soluble material, chiefly extractable from ether with potassium bicarbonate to give a fatty acid, m.p. 52–53 °C (methanol) (Found: C, 74·3; H, 12·4%. Calc. for $C_{14}H_{28}O_2$: C, 73·6; H, 12·3%. Calc. for $C_{16}H_{32}O_2$: C, 75·0; H, 12·5%). This is probably a mixture of palmitic and stearic acids. The small amount of copper salt, m.p. 92–93 °C, was dried at 60 °C/12 hr/1 mm (Found: C, 58·2; H, 7·2; OCH_3, 12·1%. Calc. for $(CH_3O)_3C_{26}H_{32}O_6Cu$: C, 59·5; H, 6·7; OCH_3, 10·9%. Calc. for $(CH_3O)_2C_{24}H_{28}O_6Cu$; C, 58·1; H, 6·3; OCH_3, 11·4%). A 1:1 mixture of these salts has the calculated analyses: C, 58·8; H, 6·5; OCH_3, 11·2%. The ultraviolet spectrum of the recovered tasmanone (ε calc. on mol. wt. 277) had the following bands: $\lambda_{max.}$ 238 mμ, log $\varepsilon_{max.}$ 4·02; $\lambda_{max.}$ 278 mμ, log $\varepsilon_{max.}$ 3·74; $\lambda_{max.}$ 323 mμ, log $\varepsilon_{max.}$ 3·77.

Sample 5 (28.v.54), a small amount of "phenolic" fraction soluble in carbonate gave a ferric colour resembling that of leptospermone rather than tasmanone; a small amount of copper salt obtained had m.p. 62–64 °C.

(*b*) *Dehydroangustione.*—(i) *Purification.* The oil of *Backhousia angustifolia* employed was that previously used for the extraction of angustifolionol (Birch, Elliott, and Penfold 1954). It appeared to contain less angustione than the sample used by Cahn *et al.* (1931) which facilitated purification. Fractional extraction with sodium bicarbonate, carbonate, and hydroxide successively was used in an endeavour to see whether other "phenolic" compounds were present, but only dehydroangustione (imine, m.p. *c.* 155 °C) and angustione (imine, m.p. *c.* 133 °C) could be identified. It is noteworthy that dehydroangustione was slowly extracted even by sodium bicarbonate solution. Repeated crystallization of dehydroangustione imine from benzene gave the pure material as massive colourless prisms, m.p. 157·5 °C $[\alpha]_D$ 0·0° (*c*, 0·02 in chloroform). The recovered dehydroangustione (Cahn *et al.* 1930) had b.p. 19 °C/1 mm, $\lambda_{max.}$ 230 mμ, log $\varepsilon_{max.}$ 4·05; $\lambda_{max.}$ 282 mμ, log $\varepsilon_{max.}$ 3·76 (ethanol), $[\alpha]_D$ 0·0° (hom.).

(ii) *Ozonolysis.* Dehydroangustione (1·6 g) in pure ethyl acetate (25 c.c.) was ozonized at 0 °C for 2 hr. No formaldehyde could be detected in the issuing gas. The residue, after reaction with zinc dust and acetic acid, was distilled into 2,4-dinitrophenylhydrazine solution. No formaldehyde derivative could be isolated. Dehydroangustione imine (3 g) similarly treated produced no formaldehyde.

(iii) *Properties of Dehydroangustione Imine and Angustione Imine.* The dehydroangustione imine had m.p. 157·7 °C $[\alpha]_D$ 0° (chloroform) (Found: C-Me, 16·3%. Calc. for $C_{11}H_{15}O_2N$ (3C-Me): 23·3%); the principal bands (λ in μ) in the infra-red ("Nujol" mull) are: 3·10s,* 3·45s, 3·95m, 6·18s, 6·4s, 6·85s, 7·34s, 7·50s, 7·9m, 8·37m, 8·8w, 9·6w, 9·75w, 10·05s, 10·3w, 10·65w, 11·34s, 11·51m, 11·9w, 12·22m, 13·07s, 13·9w. Angustione was prepared by hydrogenation of dehydroangustione (cf. Gibson, Penfold, and Simonsen 1930; Cahn *et al.* 1931). The imine had m.p. 139 °C (Found: C-Me, 16·1%. Calc. for $C_{11}H_{17}O_2N$ (3C-Me), 23·1%); the principal bands (λ in μμ in the infra-red ("Nujol" mull)) are 3·10s, 3·45s, 6·18s, 6·35s, 6·96s, 7·15m, 7·33s, 7·58s, 7·40w, 8·05s, 8·50w, 9·05w, 9·40w, 9·67w, 10·0w, 10·18w, 10·47w, 10·85w, 11·1w, 11·66w, 12·2w, 13·15m, 13·55w, 14·73w. No signs of bands were observed in the "finger-print" region of dehydroangustione imine due to angustione imine; in particular the strong band at 8·05μ due to the latter was completely absent.

* s, strong; m, medium; w, weak.

(iv) *Partial Synthesis.* 1,1,3-Trimethyl*cyclo*hex-5-en-2,4-dione was prepared from dehydroangustione according to Gibson, Penfold, and Simonsen (1930), and had m.p. 161 °C (Found: CCH_3, 11·6%. Calc. for $C_9H_{12}O_2$ (2 CCH_3): 19·7%).

This ketone (1 g) was refluxed with acetic anhydride (5 g) and anhydrous sodium acetate (0·2 g) for 4 hr. The product was decomposed with water, extracted with ether, the extract washed with sodium bicarbonate and evaporated to give an oil, b.p. 86–88 °C/1 mm which readily gave rise to dehydroangustione imine, m.p. 155 °C, undepressed by an authentic specimen, and to the copper salt of dehydroangustione, m.p. 193 °C, undepressed by an authentic specimen.

(c) *Calythrone.*—Calythrone was extracted from the oil of *Calythrix tetragona* Lab. kindly presented by Mr. A. R. Penfold, and purified through the crystalline sodium salt (Penfold and Simonsen 1940). Careful examination of the mother liquors from this insoluble salt failed to show any trace of an acylphloroglucinol derivative. The ultraviolet absorption (ethanol) between 200–420 mμ showed bands at $\lambda_{max.}$ 240 mμ, log $\varepsilon_{max.}$ 4·29 and $\lambda_{max.}$ 266 mμ, log $\varepsilon_{max.}$ 4·26.

(i) *Reduction of Calythrone.* Calythrone (500 mg) in aqueous potassium hydroxide (5%, 20 c.c.) was shaken with sodium amalgam (5%; 4 g) for 12 hr. The aqueous solution was then steam-distilled into 2,4-dinitrophenylhydrazine in 2N hydrochloric acid. The *iso*valeraldehyde 2,4-dinitrophenylhydrazone so formed had m.p. 122 °C from ethanol, undepressed by an authentic specimen (Found: C, 49·2; H, 5·2%. Calc. for $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3%).

Attempts to hydrolyse calythrone with even 10N hydrochloric acid at 100 °C merely resulted in recovery of the starting material.

(d) "*Macropone*" *from* Eucalyptus polybractea.—Commercial *E. polybractea* oil (4 gal) was extracted with 10% aqueous sodium hydroxide (500 c.c.). After acidification the oil was taken up in ether and extracted successively with sodium bicarbonate, sodium carbonate, and sodium hydroxide solution. The first two extracts yielded nothing of interest and gave no crystalline copper salts. The last extract readily gave rise to the 2,4-dinitrophenylhydrazone of 2-hydroxy-4-*iso*propylbenzaldehyde ("macropone"), m.p. 253 °C, undepressed by an authentic specimen. This fraction consisted largely of 4-*iso*propylphenol ("australol").

VII. Acknowledgments

We are indebted to Mr. A. R. Penfold for gifts of crude calythrone and dehydroangustione and for steam distillation of leaves, to Professor H. N. Barber and Dr. I. R. C. Bick for collecting *E. risdoni* and other specimens, to Dr. G. D. Meakins for advice on infra-red spectra, and to Messrs. Lockwood Magrath for a supply of *E. polybractea* oil. Part of this work was supported by a grant from the Rockefeller Foundation (New York).

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METHYLSTEROIDS

I. SOME OBSERVATIONS ON 3-METHYL-SUBSTITUTED STEROIDS DERIVED FROM CHOLESTEROL

By C. S. Barnes* and A. Palmer*

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Summary

Configurations are assigned to the epimeric 3-methylcholestan-3-ols, and their dehydration product (Farmer and Kon 1937) is shown to be 3-methylcholest-2-ene.

I. Introduction

3β-Methylcholest-5-ene was desired as a cholesterol analogue having the hydroxyl replaced by a chemically inert group. This led to a re-examination of the only previously reported 3-methylcholestene which had been prepared (Farmer and Kon 1937) by dehydration of a 3-methylcholestan-3-ol made by the action of methylmagnesium iodide on cholestanone.

The same carbinol and an isomer, both of which dehydrated to a 3-methylcholestene, have been prepared by the action of methylmagnesium iodide on cholestanone cyanohydrin (Kuwada and Miyasaka 1938). These authors did not distinguish between the alternative 2,3; 3,4; or exocyclic positions of the double bond in the olefin, nor did they determine the configurations of the isomeric carbinols. These points have now been clarified.

II. 3β-Methylcholest-5-ene

The stereochemistry of the Marker acid, cholest-5-ene-3β-carboxylic acid and its reduction product, 3β-hydroxymethylcholest-5-ene (I) has been fully discussed by Roberts, Shoppee, and Stephenson (1954).

When the tosylate (II) of this alcohol was reduced with lithium aluminium hydride by Baker, Minckler, and Petersen (1955) (see also Baker and Petersen 1951) they obtained 3β-methylcholest-5-ene (III). This was catalytically reduced to 3β-methylcholestane (IV), the β-configuration being assigned to the methyl group since no asymmetric centre was involved in the reduction.

In our hands reduction of the tosylate gave the olefin (III) having physical constants in good agreement with those obtained by Baker, Minckler, and

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Petersen (1955), as well as some of the parent alcohol (I). Similar hydrolyses of tosylates with lithium aluminium hydride have been previously observed (e.g. Schmidt and Karrer 1949). Hydrogenation of the double bond using Adams's catalyst in ethyl acetate containing a trace of perchloric acid (Hershberg *et al.* 1951) gave 3β-methylcholestane having physical constants (m.p. 103–104 °C, $[\alpha]_D$ +25°) differing somewhat from those found by Baker, Minckler, and Petersen (1955) (m.p. 97–98 °C, $[\alpha]_D$ +11°). The configuration at C5 is supported by molecular rotation evidence (Table 1), as well as by the production of 3β-methylcholestane by hydrogenation of 3-methylcholest-2-ene (VIII), which undoubtedly has *trans*-fused rings A and B.

TABLE 1

MOLECULAR ROTATION CONTRIBUTION OF THE 5,6-DOUBLE BOND

Compound	$[M]_D$ in Chloroform	Δ
Cholesterol	−154°*	−243°
Cholestanol	+89°*	
3β-Methylcholest-5-ene ..	−134°	−230°
3β-Methylcholestane ..	+96°	

* Data from Barton (1946).

III. The Epimeric 3-Methylcholestan-3-ols

By the action of methylmagnesium iodide on cholestanone and crystallization of the product, Farmer and Kon (1937) isolated a carbinol, m.p. 147–148 °C. As well as this compound, an isomeric carbinol, m.p. 125 °C, was obtained by Kuwada and Miyasaka (1938) by the action of the Grignard reagent on cholestanone cyanohydrin. These carbinols were not studied further, other than showing that both dehydrated to the same olefin.

We have examined more closely the reaction between methylmagnesium iodide and cholestanone (V) under conditions similar to those of Farmer and Kon (1937), and find that the product on chromatography is separable into two isomers of m.p. 151–152 °C and 127–128 °C. These are presumably identical with those previously recorded and have epimeric 3-hydroxyls. Distinction between the two is made by a comparison of chemical behaviour.

The compound, m.p. 127–128 °C, was eluted first from an alumina column as would be expected for the epimer with an axial hydroxyl (Savard 1953). It did not form a digitonide.

Dehydration with phosphorus oxychloride in pyridine went smoothly to give 3-methylcholestene (VIII). This ease of elimination is characteristic of an axial hydroxyl having a *trans*-axial hydrogen on the α-carbon atom, so that the four centres involved are coplanar (Barton and Rosenfelder 1951). We conclude then that the carbinol, m.p. 127–128 °C, is 3-methylcholestan-3α-ol (VI).

The compound, m.p. 151–152 °C, was eluted second from the column as would be expected for the epimer with an equatorial hydroxyl. With phosphorus

oxychloride in pyridine it gave a halogen-containing product which was not purified, since on chromatography over alumina it was converted quantitatively to the olefin (VIII).

Such behaviour is understandable if the carbinol has an equatorial hydroxyl group which is sterically unfavourable for elimination, but which undergoes substitution with inversion to give the labile 3α-chloro-compound (Heusler and Wettstein 1952). The carbinol formed a digitonide which was rather soluble in alcohol, but from which the starting material could be regenerated. We conclude that the carbinol of m.p. 151–152 °C is 3-methylcholestan-3β-ol (VII).

Farmer and Kon (1937) reported an unusual reaction during the attempted selenium dehydrogenation of the 3-methylcholestan-3-ols. Instead of the expected aromatic hydrocarbon the product was completely saturated and formulated as 3-methylcholestane. Baker, Minckler, and Petersen (1955) interpreted this result to mean that the saturated hydrocarbon had a 3β-methyl-group. We have repeated and confirmed this experiment, finding that the major product is indeed 3β-methylcholestane, with little or no aromatic hydrocarbon formed.

IV. Infra-Red Spectra

The infra-red spectra of the epimeric carbinols were examined by Dr. J. B. Willis, who reports as follows:

Cole, Jones, and Dobriner (1952) have reported strong bands near 1000 and 1040 cm^{-1} for 3α- and 3β-hydroxy*allo*steroids respectively while tertiary aliphatic alcohols show a band near 1140 cm^{-1} (Zeiss and Tsutsui 1953). In carbon disulphide solution neither carbinol showed strong absorption in the region 900–1200 cm^{-1}.

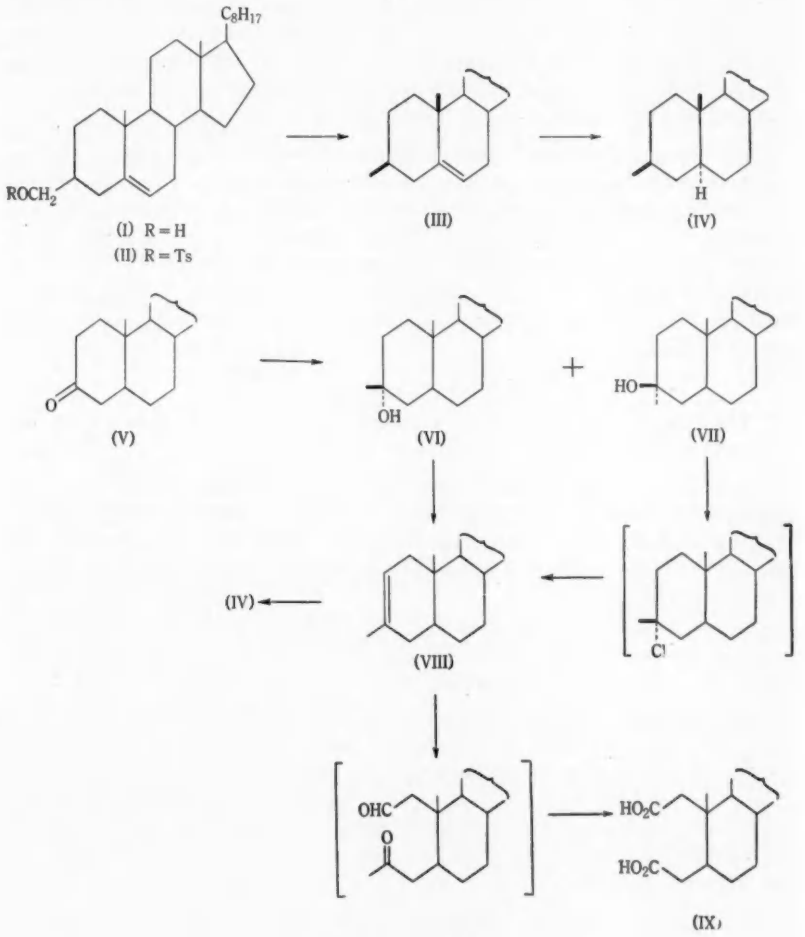
In a "Nujol" mull the compound, m.p. 127–128 °C, showed a sharp band at about 3500 cm^{-1} while the corresponding band in the spectrum of the compound, m.p. 151–152 °C, was broader and at 3330 cm^{-1}.

This suggests that the first compound exists as dimers in the solid state, while the second is present as higher polymers (Smith and Creitz 1951). From models it is seen that the compound having the more hindered 3α-(axial) hydroxyl is less free to form hydrogen bonds than its 3β-(equatorial)hydroxy-epimer, therefore the assignment of a 3α-hydroxy group to the carbinol, m.p. 127–128 °C, and a 3β-hydroxy-group to the carbinol, m.p. 151–152 °C, is also supported by the infra-red evidence.

V. 3-Methylcholest-2-ene

The olefin (VIII), m.p. 83 °C, obtained by dehydration of the epimeric 3-methylcholestan-3-ols is presumably identical with that formed similarly by Farmer and Kon (1937) and having m.p. 81–82 °C, and by Kuwada and Miyasaka (1938) and having m.p. 84 °C. Hydrogenation of VIII gave 3β-methylcholestane identical with that previously obtained by hydrogenation of 3β-methylcholest-5-ene.

The double bond was shown to be in the 2,3-position since on ozonization followed by sodium hypoiodite oxidation an acid identical with an authentic sample of Windaus' acid (IX) was obtained. It follows that the olefin (VIII) is 3-methylcholest-2-ene.



VI. Experimental

Melting points are corrected. Analyses are from the C.S.I.R.O. Microanalytical Laboratory.

(*a*) *General.*—Unless stated otherwise all rotations are measured in chloroform solution at 20±2°, and absorption spectra in ethanol. Light petroleum refers to the fraction, b.p. 60–80 °C.

(*b*) *3β-Methylcholest-5-ene* (*III*).—The *p*-toluene sulphonate of 3β-hydroxymethylcholest-5-ene (II) (0·5 g, m.p. 148–149 °C, cf. Baker and Petersen 1951) was dissolved in anhydrous

ether (200 ml) and lithium aluminium hydride (200 mg) added. After standing overnight at room temperature excess reagent was destroyed with ethyl acetate, the ethereal solution poured into dilute HCl and worked up in the usual way.

After filtering through alumina in a light petroleum (b.p. below 40 °C) solution and eluting with the same solvent, 3β-methylcholest-5-ene (0·3 g) was obtained which crystallized from acetone-methanol to have m.p. 84–85 °C, $[\alpha]_D$ −35° (*c*, 0·9) (Found: C, 87·5; H, 12·5%. Calc. for $C_{28}H_{48}$: C, 87·4; H, 12·6%).

Further elution of the column with ether gave 3β-hydroxymethylcholest-5-ene (0·1 g) which after crystallization from acetone had m.p. 129 °C, undepressed after mixing with the authentic alcohol.

(*c*) *3β-Methylcholestane* (*IV*).—The olefin (III) (100 mg) in ethyl acetate (100 ml) and perchloric acid (0·25 drop) was reduced with hydrogen using platinum oxide (100 mg) catalyst. Washing with water and evaporation of the solvent gave 3β-methylcholestane (IV) which crystallizd from acetone-methanol to have m.p. 103–104 °C, $[\alpha]_D$ +25°, +26° (*c*, 1·5, 1·3) (Found: C, 86·9; H, 13·0%. Calc. for $C_{28}H_{50}$: C, 87·0; H, 13·0%).

(*d*) *Reaction of Methylmagnesium Iodide with Cholestanone.*—The ketone (V; 10 g) in ether (75 ml) was added to a solution of methylmagnesium iodide (from methyl iodide (6 ml) and magnesium (2·5 g) in ether (25 ml)) and the solution refluxed for 3 hr. Pouring onto ice and ammonium chloride and working up in the usual way gave a gelatinous product, which was chromatographed over neutral alumina from benzene solution.

Elution with benzene gave from the first two fractions (500 ml) 3-methylcholestan-3-α-ol (VI; 6 g) which crystallized from methanol, m.p. 126–127 °C, $[\alpha]_D$ +26° (*c*, 1·0) (Found: C, 83·8; H, 12·6%. Calc. for $C_{28}H_{50}O$: C, 83·5; H, 12·5%).

After one mixed fraction (500 mg) further elution yielded 3-methylcholestan-3β-ol (VII; 4 g) crystallizing from methanol, m.p. 151–152 °C, $[\alpha]_D$ +30° (*c*, 1·7) (Found: C, 83·6; H, 12·7%).

(*e*) *Treatment of the Epimeric Carbinols with Digitonin.*—In three flasks were put samples (40 mg) of cholesterol, 3-methylcholestan-3α-ol (VI), and 3-methylcholestan-3β-ol (VII) dissolved in 95% ethanol (6 ml), and a solution (10 ml) of digitonin (1% in 90% ethanol) added to each. The cholesterol digitonide precipitated immediately but the test solutions remained clear after standing overnight. Addition of water (4 ml) to each produced a precipitate only of the digitonide of the 3-methylcholestan-3β-ol (VII). Crystallization from aqueous ethanol gave a solid of diffuse melting range above 215 °C. It was digested with pyridine and ether, and on evaporation of the ether layer obtained after centrifuging gave the carbinol (VII), m.p. 150–151 °C, undepressed on mixing with starting material.

Further addition of water (1 ml) to the solution containing carbinol (VI) caused pure starting material to crystallize having m.p. 126–127 °C, undepressed on mixing with authentic VI.

(*f*) *Reaction of the Epimeric 3-Methylcholestan-3-ols with Phosphorus Oxychloride.*—To a solution of the carbinols (0·5 g) in pyridine (15 ml) at 0 °C was added phosphorus oxychloride (1 ml) and the solution stood overnight in the refrigerator. Working up in the usual way gave from the 3α-hydroxy-compound (VI), 3-methylcholest-2-ene (VIII), which crystallized from acetone-methanol to have m.p. 82·5–83 °C, $[\alpha]_D$ +66° (*c*, 1·8) (Found: C, 87·5; H, 12·5%. Calc. for $C_{28}H_{48}$: C, 87·4; H, 12·6%).

On working up the solution from the 3β-hydroxy-compound (VII) in the usual way was obtained a solid which crystallized from acetone to have a melting range of 90–100 °C, and which gave a positive Beilstein test.

Combination of the mother liquors and crystals and filtration through alumina from light petroleum gave after one crystallization pure 3-methylcholest-2-ene (VIII), m.p. 82–83 °C, undepressed on mixing with that previously obtained.

(*g*) *Hydrogenation of 3-Methylcholest-2-ene* (*VIII*).—The olefin (VIII) was hydrogenated in the same way as its isomer III and gave 3β-methylcholestane, m.p. 100–102 °C, $[\alpha]_D$ +25° (*c*, 0·9) undepressed on mixing with that previously prepared.

(*h*) *Oxidation of 3-Methylcholest-2-ene* (*VIII*).—The olefin (VIII ; 1 g) in chloroform (50 ml) was ozonized at 0 °C until it no longer gave a colour with tetranitromethane (10 min). The solvent was removed under reduced pressure and the ozonide decomposed by boiling water for 2 hr. After cooling and pouring off the water the product was dissolved in dioxan (20 ml) and oxidized further by the addition of aqueous NaOH (2 ml ; 5%) then a solution (5 ml) of iodine (2 g) in water (20 ml) and potassium iodide (4 g) and warming on the steam-bath (10 min).

The acid fraction was sublimed and crystallized from acetone-light petroleum to give 2,3-secocholestan-2,3-dioic acid, m.p. 197–199 °C, undepressed on mixing with an authentic sample prepared by the method of Windaus and Uibrig (1914).

(*i*) *Reaction of Selenium with 3-Methylcholestan-3β-ol* (*VII*).—The carbinol (VII ; 2 g) was treated in the manner described by Farmer and Kon (1937). After decanting, the molten product crystallized, but was filtered through alumina from a light petroleum solution to remove selenium. Crystallization once from acetone gave needles, m.p. 95–97 °C (1·5 g), which were transparent in the ultraviolet region. Repeated recrystallization from acetone gave a product, m.p. 99–100 °C, $[\alpha]_D$ +25°, m.p. 102–103 °C, on mixing with authentic 3β-methylcholestane.

The combined mother liquors on evaporation had $\lambda_{max.}$ 232, 262 mμ ; $E^{1\%}_{1\,cm}$ 120, 90.

VII. Acknowledgments

We thank Dr. J. B. Willis for measuring and interpreting the infra-red spectra and Dr. A. R. H. Cole for discussion.

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THE ALKALOIDS OF *ATHEROSPERMA MOSCHATUM* LABILL.

I. ISOLATION OF THE ALKALOIDS AND STRUCTURE OF BERBAMINE

By I. R. C. Bick,* P. S. Clezy,* and W. D. Crow†

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Summary

The bark of *Atherosperma moschatum* Labill. of the family Monimiaceae contains the known bisbenzyl*iso*quinoline alkaloids berbamine (1·6 per cent.) and *iso*tetrandrine (0·06 per cent.), together with *iso*corydine (0·007 per cent.) and three new alkaloids *atherosperminine*, $C_{20}H_{23}O_2N$ (0·005 per cent.), *atherospermidine*, $C_{18}H_{13}O_4N$ (0·006 per cent.), and *spermatheridine*, $C_{17}H_{11}O_3N$ (0·002 per cent.). The last two alkaloids are bright yellow and weakly basic. In addition to the bases listed above the leaves contain a trace of another alkaloid *spermatherine*. Both bark and leaves contain phenolic alkaloids which were not further investigated. The position of the hitherto unlocated hydroxyl group in berbamine is unequivocally established by fission of *O*-ethylberbamine with sodium in liquid ammonia.

I. Introduction

Atherosperma moschatum Labill. of the family Monimiaceae, a tree of some 30 to 40 ft in height, occurs only in south-eastern Australia and is mainly found in mountain gullies. Its highly aromatic leaves‡ and bark have been used in the treatment of asthma and certain forms of heart disease (Bailey 1909); an examination of the essential oils is described by Scott (1912). The species is of some historical interest in that it was the first Australian plant from which an alkaloid was isolated (Zeyer 1861; Stockman 1892), although the amorphous base atherospermine, $C_{30}H_{40}O_5N_2$, was incompletely characterized and not chemically examined. Representatives of a number of monimiaceous genera including *Laurelia* and *Pneumus* (*Boldea*) (Henry 1949) as well as the endemic *Daphnandra* (Bick, Taylor, and Todd 1953) and *Doryphora* (Petrie 1912) have been shown to contain alkaloids, and in all cases where structures have been successfully established the alkaloids possess the familiar benzyl*iso*quinoline nucleus in one or other of its modifications.

II. Isolation and Degradation of Berbamine

The crude alkaloids from bark collected near Kallista (Vict.) and Maydena (Tas.) were freed from phenolic§ alkaloids and crystallized from benzene. The

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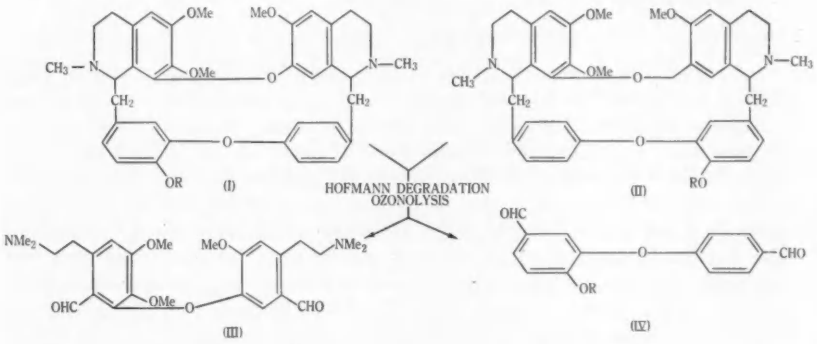
‡ The tree is commonly known as Southern sassafras.

§ The term phenolic is used throughout in a functional rather than structural sense. Thus berbamine, although it can under certain circumstances be dissolved in alkali, is readily extracted from such solutions by immiscible solvents. Cryptophenolic bases of this nature are classified in the isolation procedure as non-phenolic.

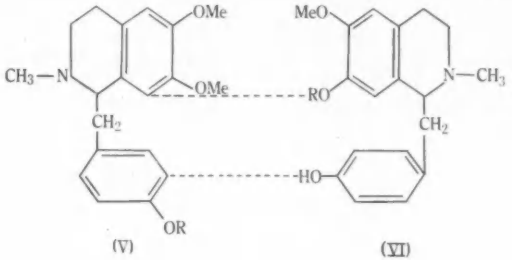
bulk of the alkaloid was thus obtained as a crystalline benzene adduct, and was later identified as berbamine, $C_{37}H_{40}O_6N_2$. Although the properties and analytical data were in agreement with those of berbamine, considerable difficulty was experienced in confirming the identity. Comparison by mixed melting point was not satisfactory due to the wide range over which melting occurs, and comparison of X-ray diffraction patterns and infra-red spectra were similarly indecisive, probably due to differences in amount of solvent of crystallization. However, both the *O*-ethyl and *O*-methyl ethers melted sharply and did not depress the melting points of corresponding derivatives of authentic berbamine.

The general features of the berbamine molecule (I; R=H) were established by von Bruckhausen, Oberempt, and Feldhaus (1933) by degradation along the lines shown below. The degradation products III and IV had also been obtained (von Bruchhausen and Gericke 1931) from the isomeric oxyacanthine (II; R=H), in which the hydroxyl group had previously been shown (Späth and Pikl 1929) to reside in one or other of the benzyl groups. Assuming that it occupied an analogous position in berbamine, von Bruchhausen, Oberempt, and Feldhaus (1933) advanced the formulae I (R=H) and II (R=H) for the two alkaloids but at that time were unable to differentiate between them.



This ambiguity was resolved by Tomita, Fujita, and Iurai (1951) who submitted *iso*tetrandrine (berbamine methyl ether; I; R=Me) to fission by sodium in liquid ammonia, a process resulting in cleavage at the diphenyl ether linkages and thus reversal of what is presumed to be the route of biosynthesis of these alkaloids. They isolated (−)-*O*-methylarmepavine (V; R=Me) and (+)-*N*-methylcoclaurine (VI; R=H), thus establishing the structure of *iso*tetrandrine as I (R=Me). The same method of degradation was applied to berbamine (I; R=H) by Inubushi (1952), who found that only one aryl ether link was split, but that the product could be methylated and the second linkage would then undergo normal fission. In this case the products isolated were (−)-*O*-methylarmepavine (V; R=Me) and (+)-*ON*-dimethylcoclaurine (VI; R=Me), showing that the lower (benzyl) ether linkage was the resistant one. Tomita, Inubushi, and Niwa (1952) had shown that *o*-hydroxydiphenyl ethers

were resistant to this fission, and on this basis Inibushi assumed that the hydroxyl group in berbamine was *ortho* to the resistant linkage. In the absence of model experiments on hydroxybisdiphenyl ethers we feel that this conclusion is open to question ; the failure to react may have been due to solubility effects. However, we have confirmed the location of the hydroxyl group as that shown (I ; R=H) by a simpler and completely unambiguous method. *O*-Ethyl-



(V) (VI)

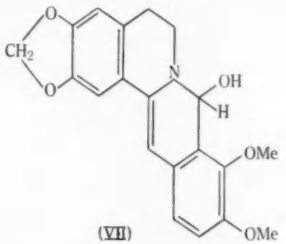
berbamine (I ; R=Et) was submitted to ether fission as described above and afforded (−)-*O*-ethylarmepavine (V ; R=Et) and (+)-*N*-methylcoclaurine (VI ; R=H). *O*-Ethylberbamine was also submitted to Hofmann degradation and ozonolysis as described for *iso*tetrandrine and gave the expected 2-ethoxydiphenyl ether-5,4′-dialdehyde (IV ; R=Et).

III. Isolation of the Minor Alkaloids

After removal of the bulk of the berbamine as the benzene adduct, the residual mixture was shown by paper chromatography to contain five other bases. When the alkaloids in benzene solution were allowed to compete for successive small portions of dilute acid some degree of separation was observed ; paper chromatography showed that an increase in basic strength corresponds to a decrease in R_F value in the *n*-butanol-acetic acid solvent used. The mixture was submitted to countercurrent distribution between chloroform and dilute hydrochloric acid in the distribution train described by Lathe and Ruthven (1951), the various fractions being grouped according to analysis by paper chromatography and subsequently purified by chromatography over alumina. The first and second groups consisted of almost pure berbamine, the strongest base present, while the third group contained the methyl ether of this base, *iso*tetrandrine. In the fourth and fifth groups were new weakly basic alkaloids designated spermatheridine, $C_{17}H_{11}O_3N$, and atherospermidine, $C_{18}H_{13}O_4N$, respectively. These two almost indistinguishable alkaloids were sparingly soluble in organic solvents, forming bright yellow-green fluorescent solutions, and gave red salts from which they were recovered unchanged. Analytical data indicate that atherospermidine is a methoxyspermatheridine ; they would seem *a priori* to be benzyl*iso*quinoline alkaloids and their low H/C ratio suggests a type of structure similar to that of berberine (VII) which they resemble in their ready reduction by zinc dust and acid to colourless compounds. The

determination of molecular weights was not possible, but the single formula is preferred because of this general similarity to berberine.

The final group, to which had been added trace constituents from other groups, contained the yellow bases together with two colourless bases. The latter were readily separated from the former by chromatography, but were not themselves separated by this means. For this purpose the cryptophenolic properties of one of them ($C_{23}H_{25}O_4N$, subsequently identified as *iso*corydine)



(VII)

was utilized. The non-phenolic constituent, atherosperminine, $C_{20}H_{23}O_2N$, crystallized only with difficulty and was isolated as the picrate. *iso*Corydine owes its presence here to the chloroform-solubility of its hydrochloride, but atherosperminine was included from previous groups.

IV. Alkaloids of the Leaves

The non-phenolic alkaloids of the leaves were examined essentially as described above. The results were very similar except in that the proportion of berbamine present was very much lower than in the bark, and that another cryptophenolic alkaloid provisionally assigned the name spermatherine was isolated in very low yield. Its probable presence in the bark was shown on re-examination of old paper chromatograms; both spermatherine and *iso*corydine have the same R_F values within experimental error, but the spots develop different colours after some days. *iso*Corydine turns green, while spermatherine develops a brownish grey colour.

V. Experimental

All melting points are corrected. Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory. Paper chromatography was carried out by the ascending method on Whatman No. 1 paper in a solvent composed of *n*-butanol-water-acetic acid in the proportions 80 : 17 : 3 by volume, and the chromatograms were printed by exposure to iodine vapour.

(*a*) *Extraction of the Bark.*—The milled bark (17·44 kg; water content 8%) was exhausted with methanol in a Soxhlet extractor and the total extract concentrated to 8 l. At this stage essential oils, waxes, and pigments were removed by extraction at 60 °C with petroleum (100–110 °C), the extracts being washed with 2% HCl to remove any basic material. The residual methanol was then removed and the residue treated with excess saturated $NaHCO_3$ solution and extracted repeatedly with chloroform. (A brown gum which separated during this process was homogenized with 5% HCl to remove occluded bases and then discarded.) The chloroform extracts were washed with 2% HCl (5 × 1 l.), the solvent replaced by benzene and extraction continued (3 × 1 l. of 5% acid) to ensure complete recovery of any weak bases.

All acid extracts were combined and the bases recovered into chloroform by basification (NH_3) and extraction, and the extracts concentrated to 2 l. At this stage phenolic bases were removed by extraction with 2% NaOH solution, and recovered by carbonation and extraction with chloroform as a dark brown gum (56 g)* which was set aside. The non-phenolic alkaloids were recovered in a similar state (330 g)* on evaporation of the original chloroform.

(*b*) *Isolation of the Non-phenolic Alkaloids.*—(i) *Berbamine.* The crude alkaloid mixture was dissolved in benzene, filtered from a little insoluble material (*A*), and allowed to cool. The benzene adduct of berbamine separated as colourless plates, m.p. 128–129 °C (decomp.). Concentration yielded further crops of the same material (total 205 g corresponding to 182 g berbamine).

(ii) *Minor Bases.* The mother liquors from the berbamine crystallization were evaporated to dryness and combined with the benzene-insolubles (*A*) in chloroform (2 l.). The solution was divided into 20 equal fractions and put through a 25-plate countercurrent distribution, using aqueous HCl (90 c.c. in each tube) of the strengths shown below as the stationary phase.

Tube No.	1–2	3–7	8–21	22–25
Acid (%)	0·125	0·25	1·0	5·0

Further quantities (30 × 50 c.c.) of chloroform were put through to assist the separation as in the development of a chromatographic column, then after each successive transfer of the mobile phase the stationary phase in the leading tube (i.e. in the order 1, 2, . . ., 25) was withdrawn and the bases recovered in the usual way into chloroform. The aliquots of mobile phase withdrawn from tube No. 25 after each transfer were reserved for examination. The fractions were examined individually by paper chromatography and grouped according to the results as shown.

Group	Tube No.	R_F Values†				
I	1–5	0·45				
II	6–15	0·44,	0·48,	0·73		
III	16–17	—	0·49,	0·72,	0·82	
IV	18–21	—	0·47,	0·74,	0·85,	0·93
V	22–25	0·68,	—	0·72,	0·83,	0·96
VI	Effluent solvent	0·68,	—	0·74,	0·85,	0·94

Group I was purified by chromatography on alumina (activity II) in chloroform, the dark decomposition products being retained at the top of the column. Crystallization of the recovered alkaloid from benzene afforded berbamine benzene adduct, m.p. 128–130 °C (decomp.) (5·6 g). The mother liquors were added to group II.

Group II was treated similarly, and after removal of the berbamine adduct (64·3 g) the residual bases were chromatographed on alumina, collecting fractions of 250 c.c.

Benzene eluted 0·23 g of R_F 0·44, 0·51.

Benzene-chloroform (3 : 1) eluted 0·77 g of R_F 0·46, 0·74.

Chloroform eluted 2·99 g of R_F 0·46, 0·74.

* Values were high due to the presence of chloroform, the complete removal of which was impracticable, owing to the decomposition of the alkaloids on prolonged heating.

† Relative intensities indicated by underlining. A value not underlined means that the spot was visible but insignificant compared to the other spots, i.e. a minor constituent.

Crystallization of the first two fractions from benzene afforded 0·74 g berbamine adduct, and the mother liquors, together with the third fraction, were added to group III.

Group III was clarified by passage through a short column of activity II alumina in chloroform and then chromatographed in benzene over the same grade of adsorbent. An amber oil (12·0 g, R_F 0·51) was rapidly eluted by benzene and subsequently crystallized from ethanol as colourless prisms of *iso*tetrandrine, m.p. 183–184 °C. The residual bases were eluted with chloroform and added to group IV. They had R_F 0·52, 0·74, 0·84.

Group IV was chromatographed over alumina in chloroform, the first colourless eluates (R_F 0·53, 0·74) being treated as for Group III. The colourless base eluted by benzene was identified as *iso*tetrandrine (0·6 g) and the chloroform eluates were added to group V. The coloured base subsequently eluted from the group IV mixture had R_F 0·83 and crystallized from pyridine or methyl cellosolve as bright yellow needles (0·43 g) of *spermatheridine*, m.p. 276–278 °C (decomp.).

Group V was chromatographed in chloroform as for the previous group, the first colourless eluates (R_F 0·68, 0·74) being added to group VI. Later eluates had R_F 0·83, 0·93 and on crystallization from pyridine afforded yellow needles (1·04 g) of *atherospermidine*, m.p. 276–278 °C (decomp.), depressed 27 °C on admixture with spermatheridine. The mother liquors were added to group VI.

Group VI was similarly treated to give a colourless mixture (VIa) and a mixture of the two yellow bases. The latter were separated by 5-plate distribution between chloroform and 1% HCl, the stronger base (spermatheridine, 0·05 g) distributing mainly into the acid. The chloroform contained 0·07 g atherospermidine. Group VIa had R_F 0·68, 0·74, and preliminary attempts at chromatography indicated that the base of R_F 0·68 might be cryptophenolic. The mixture was therefore dissolved in the minimum amount of 0·25% HCl and poured rapidly into a large excess of 1% NaOH solution. The insoluble material filtered off was substantially pure, and on repeating the process several times a full separation was achieved. The insoluble base (0·85 g) had R_F 0·73 and crystallized only with difficulty from acetone-petroleum (60–70 °C) to give colourless needles of *atherosperminine*, m.p. 199 °C. Recovery of the cryptophenolic base from the alkaline solutions afforded *iso*corydine (1·21 g), which crystallized from methanol as colourless prisms, m.p. 183–184 °C.

(*c*) *Isolation of the Bases from the Leaves.*—The crude alkaloids from the leaves (8·85 kg), obtained as described above, were separated into phenolic (5·0 g) and non-phenolic (20·0 g) fractions. The latter was submitted to countercurrent distribution as described for the bark alkaloids, in this case using 75 c.c. stationary phase in each tube.

Tube No.	Strength of Acid (%)	Fractions		
		Group No.	Tubes	R_F Values
1–5	0·01	I	1–12	0·36–48, 0·59, 0·73
6–15	0·10	II	13–20	0·61
16–20	0·50	III	21–25	0·61, 0·83
21–23	1·00	IV	Effluent	0·83, 0·91
24–25	5·00			

Group III was separated by fractional extraction with 0·05% HCl, the stronger base of R_F 0·61 being added to group II and the weaker yellow base to group IV. Group II then contained only *iso*corydine which crystallized from methanol as prisms m.p. 183–184 °C. Group IV was separated by countercurrent distribution between chloroform and 1% HCl as described previously into spermatheridine and atherospermidine.

Group I was dissolved in benzene and chromatographed on alumina. Benzene rapidly eluted *iso*tetrandrine, the major base present in the leaves, while further elution with benzene-chloroform mixtures afforded a mixture of bases of R_F 0·61 and 0·74. These bases were separated as described under Section (*b*) (ii) (group VI) into atherosperminine and a new cryptophenolic alkaloid *spermatherine*, R_F 0·61. Only a small amount was obtained, so no further examination was possible, but the material crystallized from acetone-petroleum (60–80 °C) as needles, m.p. 124–125 °C and decomposed to a brown mass on exposure to light. Final elution of the column with chloroform afforded a little berbamine, identified (as were all other substances) by comparison with an authentic specimen from the bark.

(*d*) *Characterization and Identification of the Alkaloids.*—(i) *Berbamine* from leaves or bark crystallized from benzene in colourless plates of the benzene adduct, m.p. 129–134 °C (decomp.) (Found : C, 75·0 ; H, 6·7 ; O, 13·9 ; N, 4·2 ; CH_3O, 13·8 ; CH_3N, 7·9%. Calc. for $C_{37}H_{40}O_6N_2.C_6H_6$: C, 75·2 ; H, 6·7 ; O, 14·0 ; N, 4·1 ; $3\times CH_3O$, 13·6 ; $2\times CH_3N$, 8·5%). Kondo *et al.* (1938) report $C_{37}H_{40}O_6N_2.1\frac{1}{2}C_6H_6$, m.p. 127 °C. The base was also obtained as the monohydrate which crystallized from aqueous ethanol as colourless plates sintering at 147 °C (Found : C, 71·4 ; H, 6·7%. Calc. for $C_{37}H_{40}O_6N_2.H_2O$: C, 71·2 ; H, 6·7%). Heating the benzene adduct briefly at 150 °C under reduced pressure afforded the alkaloid as a clear gum which after powdering coalesced and gradually melted from 145–155 °C (Found : C, 72·9 ; H, 6·5 ; N, 4·6 ; CH_3O, 14·6%. Calc. for $C_{37}H_{40}O_6N_2$: C, 73·0 ; H, 6·6 ; N, 4·6 ; $3\times CH_3O$, 15·1%). The alkaloid had $[\alpha]_D^{20}$ +114·6° (*c*, 1·0 in chloroform), R_F 0·47, pK_a 7·33 at 20 °C in 70% aqueous methanol and was cryptophenolic. The dihydrochloride crystallized from 2% HCl as colourless needles of the heptahydrate, m.p. 257–258 °C (decomp.) (Found : C, 54·9 ; H, 6·9 ; N, 3·5 ; Cl, 9·1%. Calc. for $C_{37}H_{40}O_6N_2.2HCl.7H_2O$: C, 55·0 ; H, 7·0 ; N, 3·5 ; Cl, 8·8%), and had $[\alpha]_D^{20}$ +64·2° (*c*, 1·0 in water). Santos (1929) records a rotation of +63·2° for the tetrahydrate. The dimethiodide crystallized from methanol-acetone as colourless needles, m.p. 287–289 °C (decomp.) (Found : C, 51·2 ; H, 5·3 ; N, 3·0 ; I, 27·5%. Calc. for $C_{37}H_{40}O_6N_2.2CH_3I.H_2O$: C, 51·0 ; H, 5·3 ; N, 3·1 ; I, 27·9%). Identification of the base was achieved by comparison of the *O*-methyl and *O*-ethyl ethers, which had sharp m.p.'s, with the corresponding derivatives prepared from authentic berbamine.

(ii) iso*Tetrandrine* crystallized from methanol as colourless prisms, m.p. 182–183 °C (Found : C, 73·2 ; H, 7·0 ; N, 4·5 ; CH_3O, 20·1%. Calc. for $C_{38}H_{42}O_6N_2$: C, 73·3 ; H, 6·8 ; N, 4·5 ; $4\times CH_3O$, 20·0%), undepressed by admixture with an authentic specimen, and had R_F 0·51, $[\alpha]_D^{20}$ +150·7° (*c*, 0·85 in chloroform). It showed no cryptophenolic properties.

(iii) iso*Corydine* crystallized from acetone-petroleum (60–80 °C) as colourless prisms (developing a pink colour on exposure), m.p. 183–184 °C (Found : C, 70·6 ; H, 6·8 ; N, 3·6 ; CH_3O, 26·9 ; act. H, 0·28%. Calc. for $C_{20}H_{23}O_4N$: C, 70·4 ; H, 6·7 ; N, 4·1 ; $3\times CH_3O$, 27·2 ; $1\times$act. H, 0·29%). The base was cryptophenolic, but showed no ferric chloride colour, and had R_F 0·68, the spot turning a characteristic green colour after some hours' exposure. The methiodide crystallized from methanol as colourless needles, m.p. 232–234 °C (decomp., green melt) alone or in admixture with an authentic specimen. Both methiodides had R_F 0·46.

(iv) *Atherosperminine* crystallized from acetone-petroleum (60–80 °C) as colourless needles m.p. 199–200 °C, but could not be satisfactorily recrystallized. The *picrate* crystallized from acetone-methanol as orange or red (interconvertible) needles, m.p. 189–190 °C (Found : C, 58·4 ; H, 4·9 ; O, 26·7 ; N, 9·8 ; CH_3O, 12·0%. Calc. for $C_{20}H_{23}O_4N.C_6H_3O_7N_3$: C, 58·4 ; H, 4·9 ; O, 26·7 ; N, 10·4 ; $2\times CH_3O$, 11·5%), while the *perchlorate* crystallized from 50% aqueous ethanol as flat cream needles, m.p. 195–196 °C (Found : C, 58·9 ; H, 6·1 ; Cl, 8·7 ; CH_3O, 15·4%. Calc. for $C_{20}H_{23}O_4N.HClO_4$: C, 58·6 ; H, 5·9 ; Cl, 8·7 ; $2\times CH_3O$, 15·1%). The base was not cryptophenolic, had R_F 0·74, and gave no methylenedioxy test.

(v) *Spermatheridine* crystallized from chloroform in bright yellow needles, m.p. 276–278 °C (decomp.) (Found : C, 74·0 ; H, 4·0 ; O, 17·1 ; N, 5·1% ; CH_3O, nil ; CH_3N, nil. Calc. for $C_{17}H_{11}O_3N$: C, 73·6 ; H, 4·0 ; O, 17·3 ; N, 5·0%) and afforded an orange-red *hydrochloride* from 5% HCl as needles, m.p. 289–292 °C (decomp.) (Found : C, 65·2 ; H, 3·3 ; N, 4·0. Calc. for $C_{17}H_{11}O_3N.HCl$: C, 65·1 ; H, 3·8 ; N, 4·4%). No phenolic or cryptophenolic groups were

found and the Labat methylenedioxy test could not be applied due to the intense red colour with H_2SO_4 alone. The alkaloid had R_F 0·83 and was readily reduced by zinc dust in acetic acid to a colourless solution with an intense blue fluorescence.

(vi) *Atherospermidine* crystallized from chloroform or pyridine as yellow needles, m.p. 276–278 °C (decomp.) (Found: C, 70·5; H, 3·9; O, 20·8; N, 3·9; CH_3O, 10·2%; CH_3N nil. Calc. for $C_{18}H_{13}O_4N$: C, 70·4; H, 4·3; O, 20·8; N, 4·6; $1\times CH_3O$, 10·1%), and gave a scarlet *hydrochloride* from 5% HCl as needles, m.p. 256–258 °C (decomp.) (Found: C, 63·0; H, 4·0; N, 4·1%. Calc. for $C_{18}H_{13}O_4N.HCl$: C, 62·9; H, 4·1; N, 4·1%). As before no phenolic groups were detected and the methylenedioxy test was not applicable. The base had R_F 0·89 and reacted towards zinc dust in acetic acid in the same way as spermatheridine.

(*e*) *Structural Examination of Berbamine.*—(i) O-*Methylberbamine.* (1) Via *berbamine-N-oxide.* Berbamine (5·0 g) in acetone (50 c.c.) was treated with 30% hydrogen peroxide (1 c.c.) and allowed to stand for 10 days, similar additions of hydrogen peroxide being made every 2 days. Evaporation of the solution under reduced pressure afforded the *N*-oxide as a colourless hygroscopic mass. Since it could not be obtained in a state suitable for analysis its identity was checked by reduction to berbamine (m.p. and mixed m.p.) with zinc and 5% HCl. The *N*-oxide (4 g) was stirred at room temperature for 16 hr with 1% NaOH (100 c.c.) and freshly distilled dimethyl sulphate (1 c.c.), the excess dimethyl sulphate removed by extraction with ether, and the residual solution reduced as described above. The regenerated base, after purification by chromatography over alumina in benzene afforded *O*-methylberbamine (0·99 g) as colourless prisms, m.p. 182 °C (Found: C, 72·9; H, 6·7; N, 4·6; CH_3O, 19·7%. Calc. for $C_{38}H_{42}O_6N_2$: C, 73·3; H, 6·8; N, 4·5; $4\times CH_3O$, 19·9%), undepressed by admixture with an authentic sample of *iso*tetrandrine. The base had $[\alpha]_D^{20}$ +144° (*c*, 0·5 in chloroform).

(2) *With diazomethane.* To a methanolic solution of berbamine (1 g in 30 c.c.) was added ethereal diazomethane (from 2 g nitrosomethylurea) and the whole allowed to stand for 6 days, two further additions of diazomethane being made at intervals of 2 days. Recrystallization of the recovered base from acetone afforded *iso*tetrandrine (0·9 g) as colourless prisms, m.p. 181–182 °C alone or in admixture with an authentic sample.

(ii) O-*Ethylberbamine.* This compound was prepared by the use of diazoethane, exactly as described for the methyl ether above. The reaction mixture was extracted with 1% HCl and the product freed from unreacted berbamine by precipitation with 1% NaOH solution. Crystallization of the precipitate from a small volume of ether and then from methanol gave *O-ethylberbamine* as colourless prisms, m.p. 186–188 °C, $[\alpha]_D^{20}$ +129° (*c*, 0·5 in chloroform) (Found: C, 73·6; H, 6·9; O, 15·6; N, 4·7%. Calc. for $C_{39}H_{44}O_6N_2$: C, 73·6; H, 7·0; O, 15·1; N, 4·4%).

(iii) *Fission of* O-*Ethylberbamine.* *O*-Ethylberbamine (0·8 g) was dissolved in toluene (10 c.c.) and liquid ammonia (300 c.c.), and clean sliced sodium (2 g) added gradually with vigorous stirring until the blue colour of the solution persisted for 1 hr, when the ammonia was allowed to evaporate and the residual solution was treated with ether and water. The organic layer was washed with 1% NaOH solution (combined with the aqueous layer) and exhaustively extracted with 1% HCl. Recovery of the non-phenolic base from the acid extracts and subsequent purification by chromatography over alumina in benzene afforded a light yellow oil (0·36 g), which was warmed with methanolic methyl iodide. (—)-*O*-Ethylarmepavine methiodide separated as colourless needles, m.p. 195–197 °C, $[\alpha]_D^{18}$ —80·1° (*c*, 0·3 in ethanol) (Found: 54·3; H, 6·3; O, 10·7%. Calc. for $C_{21}H_{27}O_3N.CH_3I.\frac{1}{4}H_2O$: C, 54·2; H, 6·3; O, 10·7%), undepressed by admixture with a specimen prepared from authentic (—)-armepavine by ethylation and quaternization. A marked depression was observed with (—)-*O*-methylarmepavine methiodide obtained from a similar fission of *iso*tetrandrine. The phenolic base recovered from the aqueous alkaline layer above was methylated with diazomethane (3 days, repeated addition of reagent) and similarly converted to the methiodide. Crystallization from methanol afforded (+)-*O*-methylarmepavine methiodide as colourless needles, m.p. 134 °C (Found: C, 51·5; H, 6·6%. Calc. for $C_{20}H_{25}O_3N.CH_3I.H_2O$: C, 51·7; H, 6·6%), $[\alpha]_D^{18}$ +120·1° (*c*, 0·3 in methanol) and did not depress the m.p. of an authentic specimen.

(iv) O-*Ethylberbamine Dimethiodide.* Berbamine (5 g) in methanol (2 l.) was refluxed with methyl iodide (5 c.c.) for 15 min and the whole evaporated to dryness under reduced pressure. The crude methiodide was dissolved in ethanol (500 c.c.) and refluxed 36 hr with ethyl iodide (12·5 c.c.) and sodium ethoxide (0·9 g sodium in 10 c.c. ethanol), similar additions being made at 6-hr intervals. The solvent was replaced by water, boiled with a little copper powder and activated charcoal, filtered, and set aside. O-*Ethylberbamine dimethiodide* separated out as a colourless powder which could not be induced to crystallize.

(v) O-*Ethylberbamine Methines.* The dimethiodide above (5 g) in water (1·5 l.) was shaken with freshly prepared silver oxide till free from iodide ion and the solution concentrated under reduced pressure to 100 c.c. Aqueous KOH (50 c.c. ; 50%) was added and the solution warmed on a steam-bath, the insoluble oil which separated being removed by chloroform extraction at intervals of 2 hr until no more was obtained. The combined extracts were washed, dried, and evaporated, yielding an amorphous resinous product.

(vi) *2-Ethoxydiphenyl Ether-5,4'-dialdehyde.* The mixture of methine bases (2 g) in 5% H_2SO_4 (20 c.c.) was ozonized in a freezing mixture for 5 min, extracted with ether, and the process repeated until no more solid was obtained. The combined extracts were washed with sodium carbonate solution, dried, and evaporated. Crystallization of the residue from petroleum (60–80 °C) afforded the dialdehyde as colourless needles (0·2 g), m.p. 59 °C (Found : C, 70·9 ; H, 5·5 ; CH_3O, 16·8%. Calc. for $C_{15}H_{12}O_4$: C, 71·1 ; H, 5·2 ; C_2H_5O (calc. as methoxyl), 16·7%), undepressed by admixture with an authentic specimen. There was a marked depression with a sample of the corresponding methyl ether.

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THE COUMARINS OF *HALFORDIA SCLEROXYLA* F. MUELL.

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Summary

The bark of *Halfordia scleroxyla* F. Muell. has been found to contain the known coumarin xanthoxyletin and two new isomeric furocoumarins of formula $C_{14}H_{12}O_6$ which have been named halfordin and *iso*halfordin. By degradation, halfordin is shown to possess structure (Ia) or (Ib) and *iso*halfordin structure (Va) or (Vb). This constitutes the first recorded isolation of the 3-methoxyfurocoumarin system from natural sources.

I. INTRODUCTION

Halfordia scleroxyla F. Muell. is a rain-forest tree of millable size which grows in northern Queensland. Engler and Prantl (1931) place the genus *Halfordia* in the subtribe Toddaliinae of the family Rutaceae. *H. kendack* F. Muell., the only other member of the genus, is similar to *H. scleroxyla* in appearance and grows in south-eastern Queensland and in New Caledonia. The barks of both species were examined for the presence of alkaloids as part of a general investigation of the family Rutaceae but no significant quantity of basic material could be found.

II. ISOLATION AND CHARACTERIZATION OF THE COUMARINS

The bark of *H. scleroxyla* has been found to contain three crystalline compounds. One of these has formula $C_{15}H_{14}O_4$ and has been identified as xanthoxyletin (5-methoxy-6,7-(2′,2′-dimethylpyrano-5′,6′)-coumarin) by its melting point and ultraviolet absorption spectrum and by the preparation of a monobromo-derivative. Xanthoxyletin was originally isolated from the bark of *Xanthoxylum americanum* by Staples (1829) and its structure determined by Bell, Robertson, and Subramanian (1936). Recently Briggs and Locker (1951) isolated it from *Melicope ternata* (Rutaceae) and King, Housley, and King (1954) have reported its presence in East Indian satinwood (*Chloroxylon swietenia*).

The other two crystalline compounds are isomers of formula $C_{14}H_{12}O_6$ and have been named halfordin (m.p. 136–137 °C) and *iso*halfordin (m.p. 151–152 °C). The crude mixture obtained from a light petroleum extract of the bark was first separated by fractional crystallization and by chromatography on activated alumina, but a more satisfactory separation was obtained by acidifying an alkaline solution of the mixture. Xanthoxyletin was rapidly regenerated, *iso*halfordin more slowly, and halfordin was converted to halfordic acid. The bark of *H. kendack* contained only halfordin.

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III. Structure of Halfordin

Halfordin is optically inactive and contains three methoxyl groups. It is insoluble in aqueous sodium carbonate but dissolves slowly in hot aqueous sodium hydroxide to give a yellow solution which yields an acid, $C_{14}H_{14}O_7$, on acidification. These solubility tests point to a coumarin structure in halfordin and the degradation studies to be described here support this conclusion. However, it should be pointed out that halfordin behaves abnormally in giving a stable *o*-hydroxycinnamic acid on acidifying its solution in sodium hydroxide. This acid which has been named halfordic acid did not cyclize to the original coumarin even on long standing in acid solution, or when dissolved in methanol and irradiated with ultraviolet light for long periods (Gruber 1944). Treatment of both halfordin and halfordic acid with dimethyl sulphate and alkali gave methyl halfordic acid, $C_{15}H_{16}O_7$, m.p. 180–181 °C which contains four methoxyl groups and one carboxyl group. Alkaline hydrogen peroxide oxidized halfordin to furan-2,3-dicarboxylic acid, indicating the presence of a furocoumarin structure in halfordin. As no methoxyl group is attached to the furan ring, only four positions remain where the three methoxyl groups can be attached. Two of these are on the benzene nucleus, and two on the pyrone ring. The similarity between the absorption spectrum of halfordin (Fig. 1) and that of the dimethoxyfurocoumarin *iso*pimpinellin (Caldwell and Jones 1945) suggests that two of the methoxyl groups are attached to the benzene nucleus so that the remaining methoxyl must be attached at either position 3 or position 4 of the pyrone ring.

Halfordin was partially demethylated in boiling hydrochloric acid giving norhalfordin, $C_{13}H_{10}O_6$, m.p. 228 °C, which was soluble in 2N sodium carbonate and was converted to halfordin with diazomethane. An alcoholic solution of norhalfordin gave with ferric chloride an immediate weak green colouration which increased in intensity on standing, characteristic of 3-hydroxycoumarins (Späth and Dobrovolny 1938 ; Jones *et al.* 1949 ; Dean, Robertson, and Whalley 1950), whereas 4-hydroxycoumarins gave a characteristic red-brown ferric colouration. Furthermore, norhalfordin failed to condense with formaldehyde under conditions which readily produce dicumarol from 4-hydroxycoumarin.

Hydrogenation of halfordin in the presence of Adams's catalyst or palladium charcoal gave dihydrohalfordin, $C_{14}H_{14}O_6$, m.p. 144–145 °C. Though halfordin contains two ethylenic linkages, no tetrahydro-derivative could be obtained, even though a number of catalysts were used at various temperatures and pressures. The difficulty experienced by Späth, Simon, and Lintner (1936) in hydrogenating coumarins with a methoxyl or acetoxyl substituent on either carbon atom 3 or 4 and the failure of sodium amalgam to reduce halfordin suggested that in dihydrohalfordin the 2′,3′-furan double bond is saturated, but the 3,4 double bond in the coumarin nucleus is still present, and this is supported by both chemical and spectroscopic evidence. Dihydrohalfordin also demethylated smoothly in boiling hydrochloric acid and the resulting nor-dihydrohalfordin gave the same green ferric colour reaction as did norhalfordin, and formed an acetate identical with that obtained by hydrogenation of the acetate of norhalfordin. It is well known (Goodwin and Pollock 1954) that

saturation of the 3,4 double bond in the coumarin nucleus greatly reduces the absorption at wavelengths longer than 300 mμ. However, conversion of halfordin to dihydrohalfordin resulted in a marked increase in the absorption at 320 mμ (Fig. 1) showing that the 3,4 double bond has not been saturated.

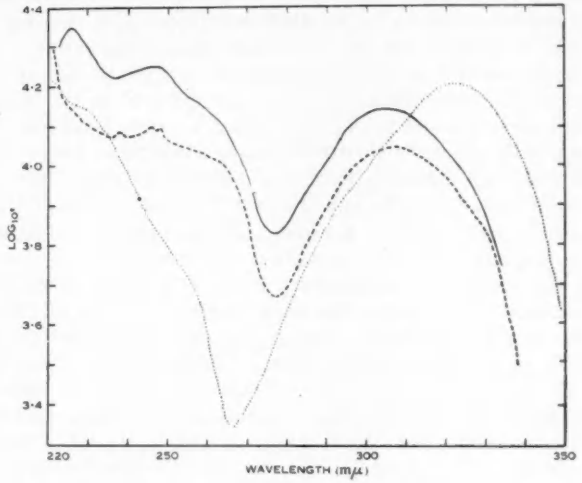
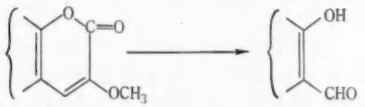


Fig. 1.—Ultraviolet absorption spectra.
——— Halfordin.
- - - - - Norhalfordin.
····· Dihydrohalfordin.

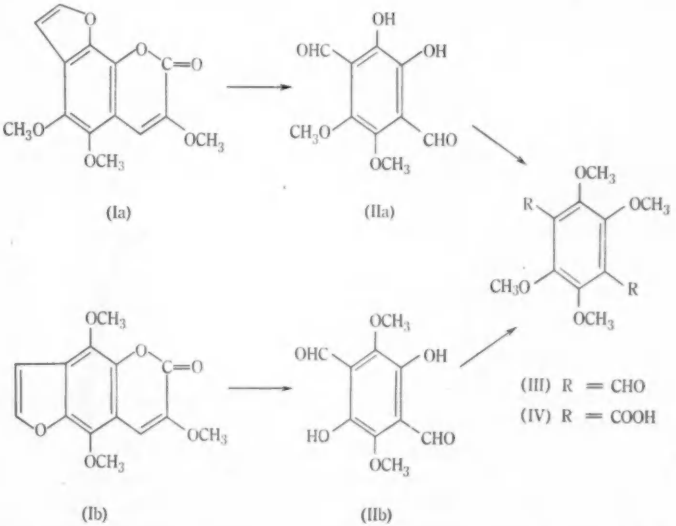
The presence of a 3-methoxycoumarin system in halfordin is implied by these experiments and was finally proved by the ozonolysis of dihydrohalfordin to a phenolic aldehyde, $C_{11}H_{12}O_5$, m.p. 105–106 °C, which contains two methoxyl groups. The elimination of three carbon atoms in the formation of this phenolic aldehyde can only be explained by placing the methoxyl group at position 3 on the coumarin nucleus as represented by the following partial formulae :



Ozonolysis of halfordin under mild conditions gave a phenolic aldehyde, $C_{13}H_{12}O_7$, m.p. 169–170 °C, containing three methoxyl groups. Only one carbon atom is lost in this oxidation which must involve fission of the furan ring as follows :

This is in agreement with the results of Späth, Platzer, and Schmid (1940). Prolonged ozonolysis of halfordin caused rupture of both furan and pyrone rings and gave a diphenolic dialdehyde, $C_{10}H_{10}O_6$, m.p. 118 °C which contained two methoxyl groups and was not volatile in steam. Methylation of this compound with methyl iodide and potassium carbonate in acetone gave a tetramethoxydialdehyde, $C_{12}H_{14}O_6$, m.p. 114–115 °C, which failed to give a colour on acidification of its ammoniacal solution with dilute acetic acid, claimed by Grove (1952) to be a specific test for *o*-phthalaldehydes. Permanganate oxidation of this compound gave a tetramethoxydicarboxylic acid, $C_{12}H_{14}O_8$, m.p. 277–280 °C (decomp.).

Tetramethoxy-*o*-phthalic acid has recently been prepared by Vischer (1953) and its melting point (178–180 °C after resetting at 135–137 °C) and properties are quite different from those of the acid, m.p. 277–280 °C, from halfordin. In work to be described later in this paper, tetramethoxy*iso*phthalic acid is prepared by degradation and synthesis and is likewise not identical with the



acid, m.p. 277–280 °C, which must therefore be tetramethoxyterephthalic acid. The high melting point is also in keeping with its being a terephthalic acid. Two structures (Ia) and (Ib) can give rise to tetramethoxyterephthalic acid by the above series of reactions and as yet no evidence is available to decide which of these represents halfordin.

IV. Structure of *iso*Halfordin

*iso*Halfordin resembles halfordin in crystalline form and has very similar solubility in most organic solvents. The ultraviolet absorption spectrum of *iso*halfordin (Fig. 2) closely resembles that of halfordin (Fig. 1). *iso*Halfordin

dissolves slowly in hot aqueous alkali, but unlike halfordin is regenerated when the solution is acidified.

At the outset it was believed that the isomerism shown by halfordin and *iso*halfordin was of the type normally found among furocoumarins and that they were related in the same way as are pimpinellin and *iso*pimpinellin (Sethna and Shah 1945). However, methylation of *iso*halfordin with dimethyl sulphate and alkali gave methyl *iso*halfordinic acid, $C_{15}H_{16}O_7$, m.p. 138–139 °C, which was isomeric with methylhalfordic acid. Its melting point was not affected by repeated crystallization or by heating at 142 °C for a short time, so the difference was not due to geometric isomerism.

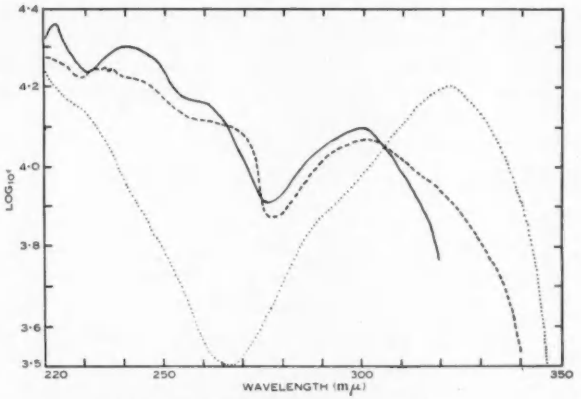
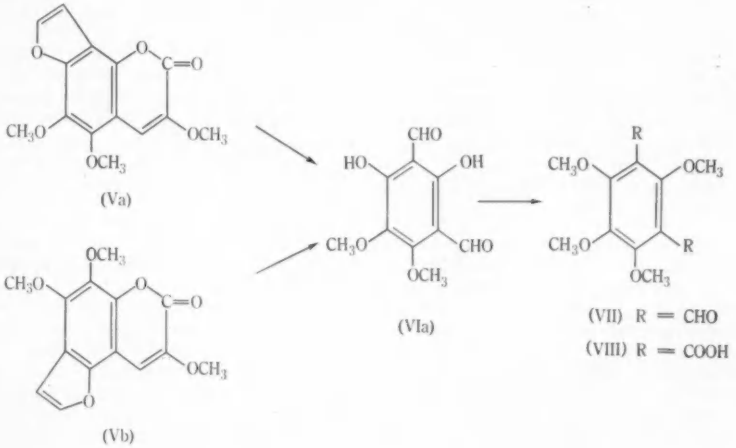


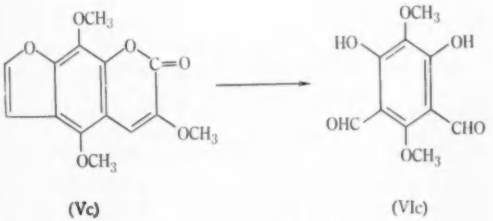
Fig. 2.—Ultraviolet absorption spectra.
——— *iso*Halfordin.
- - - - - Nor*iso*halfordin.
····· Dihydrohalfordin.

*iso*Halfordin gave furan-2,3-dicarboxylic acid on alkaline peroxide oxidation, and was demethylated, though less readily than halfordin, to nor*iso*halfordin, $C_{13}H_{10}O_6$, m.p. 200–201 °C, which resembled *nor*halfordin in giving an immediate weak green ferric reaction and being readily methylated and acetylated. Hydrogenation of *iso*halfordin gave only dihydro*iso*halfordin, $C_{14}H_{14}O_6$, m.p. 160–161 °C, and sodium amalgam failed to reduce *iso*halfordin. Dihydro-*iso*halfordin dissolved in alkali and was regenerated when the solution was acidified, proving that it contained an unsaturated coumarin system. If a dihydrocoumarin system had been present, the resulting *o*-hydroxydihydrocinnamic acid would not have lactonized spontaneously (Sethna and Shah 1945).

When *iso*halfordin was submitted to a series of degradation experiments, similar to those previously described for halfordin, further similarity was observed between these two coumarins. Ozonolysis of dihydro*iso*halfordin gave a phenolic aldehyde, $C_{11}H_{12}O_5$, m.p. 88–89 °C. Mild ozonolysis of *iso*halfordin gave a phenolic aldehyde, $C_{13}H_{12}O_7$, m.p. 139–140 °C, and prolonged ozonolysis

gave a mixture of products from which a steam volatile diphenolic dialdehyde, $C_{10}H_{10}O_6$, m.p. 114–115 °C, and the corresponding diphenolic aldehydo-acid, $C_{10}H_{10}O_7$, were isolated. Methylation of the diphenolic dialdehyde, followed by oxidation with alkaline potassium permanganate, gave tetramethoxy*iso*-phthalic acid, which was identified by comparison with a synthetic sample and was not identical with the acid similarly obtained from halfordin. The isomerism of halfordin and *iso*halfordin must therefore be due to a different arrangement of the oxygen atoms on the benzene nucleus, halfordin being a derivative of 1,2,4,5- and *iso*halfordin a derivative of 1,2,3,5-tetrahydroxy-benzene.





Three structures (Va), (Vb), and (Vc) could give rise to tetramethoxy*iso*-phthalic acid by the above series of reactions. Structure (Vc) is excluded as a possible structure for *iso*halfordin since the corresponding diphenolic dialdehyde (VIc), by analogy with the work of Baker (1934) on the isomeric diacetyl-resorcinols, would not be expected to be readily volatile in steam, whereas the product from *iso*halfordin is readily steam volatile. No evidence is yet available to decide between structures (Va) and (Vb) for *iso*halfordin, but structure (Va) is favoured since this arrangement of furan and pyrone rings has previously

been found to occur in nature. On the basis of this structure (Va) *iso*halfordin would be 3-methoxypimpinellin.

This appears to be the first recorded isolation of compounds containing the 3-methoxyfurocoumarin structure from natural sources. Furthermore, this is the only example of isomerism of this type in the furocoumarin series, where the isomerism is not due simply to different positions of the pyrone ring on a common nucleus.

V. Experimental

All melting points are corrected, except where otherwise stated.

(*a*) *Extraction of* H. scleroxyla *Bark.*—The following is an example typical of the many extractions carried out in this investigation. The dried, milled bark (3 kg) was extracted with light petroleum (Soxhlet) for 12 hr and the dark green extract concentrated to 3 l. and kept at room temperature for 3 days. The crystalline solid (fraction *A*, 9 g) was filtered off and the filtrate concentrated to 2 l. The greenish crystals which formed after 6 days were filtered off (fraction *B*, 6 g) and the mother liquor concentrated to 1 l. giving fraction *C* (15 g). The various fractions were fractionally crystallized from methanol, giving small amounts of the three pure coumarins. Fraction *A* gave *halfordin* (3 g), m.p. 136–137 °C; fraction B, iso*halfordin* (0·8 g), m.p. 151–152 °C; and fraction C, xanthoxyletin (3 g), m.p. 131–132 °C. However, most of the crystalline solid proved to be a mixture of all three coumarins.

(*b*) *Separation of Halfordin,* iso*Halfordin, and Xanthoxyletin.*—(i) *By Chromatography.* A solution of the crystalline, mixed product (5 g) in 200 c.c. light petroleum (b.p. 40–60 °C)-benzene (2 : 1) was poured on a column of neutralized, activated alumina (32 × 2 cm), and the chromatogram developed with the same solvent mixture. An ultraviolet lamp was used to follow the movements of the bands. The first band eluted had a sky blue fluorescence and proved to be xanthoxyletin (1·0 g), m.p. 131–132 °C. The second band had deep blue fluorescence and was eluted with light petroleum-benzene (1 : 1) giving 2·5 g of white needle-like crystals, m.p. 105–125 °C. The column was then washed with benzene (300 c.c.) and 600 c.c. benzene-chloroform (2 : 1) and the combined eluates gave *iso*halfordin (1·1 g), m.p. 150–151 °C. The intermediate fractions of poor melting point were combined and rechromatographed on a fresh column of alumina but the material recovered, m.p. 110–125 °C, gave no immediate colour with concentrated H_2SO_4 and consisted of a mixture of halfordin and *iso*halfordin.

(ii) *By Alkali Method.* The mixed crystalline product (10 g) in methanol (150 c.c.) was added in small portions to 3% KOH (200 c.c.) at 75 °C. The alcohol was removed under reduced pressure and the brown solution extracted with a small amount of ether to remove oily material. The ice cold aqueous layer was acidified with 15% HCl (15 c.c.) and after 45 min was thoroughly extracted with ether. The ether layer after washing with 20% Na_2CO_3 (200 c.c.) was dried and gave xanthoxyletin (1·5 g). The Na_2CO_3 solution was acidified, kept overnight in the refrigerator, and extracted with ether. The ether solution was washed with 20% Na_2CO_3 and on working up in the usual way gave *iso*halfordin (3·8 g). The carbonate layer was concentrated to 200 c.c. and methylated with dimethyl sulphate and alkali as in (*f*) to give methylhalfordic acid, m.p. 180–181 °C, which was used as starting material for various oxidation experiments.

(*c*) *Xanthoxyletin.*—Xanthoxyletin crystallized from methanol as colourless, highly refracting prisms, m.p. 131–132 °C (lit. 132–133 °C), which gave an immediate orange-red colour with concentrated H_2SO_4 (Found: C, 69·6; H, 5·4; CH_3O, 11·3%; mol. wt. (Reiche), 255. Calc. for $C_{15}H_{14}O_4$: C, 69·8; H, 5·5; CH_3O, 12·0% (one methoxyl); mol. wt., 258). The absorption spectrum of xanthoxyletin was measured in a M/20 000 ethanolic solution and showed absorption peaks at (log ε in parenthesis) 227 mμ (4·28); 269 mμ (4·32); 322 mμ (3·99); 347 mμ (4·05), which are in exact agreement with Briggs and Locker's (1951) observations. Bromoxanthoxyletin, prepared according to the method of Briggs and Locker (1951), crystallized from aqueous methanol as colourless plates, m.p. 156–157 °C (lit. 157–158 °C), and with concentrated H_2SO_4 gave the unusual colour reaction described by these authors.

(*d*) *Halfordin.*—Halfordin crystallized from methanol as white needles arranged radially in groups of four. It is very sparingly soluble in light petroleum and moderately soluble in cold ethanol, methanol, benzene, and ethyl acetate. An ethanolic solution of halfordin has a blue fluorescence but does not give a ferric colouration. Halfordin does not give an immediate colour with H_2SO_4 but dissolves to a yellow solution which does not fluoresce (Found: C, 60·7; H, 4·3; CH_3O, 33·6% mol. wt. (Reiche), 278; by titration, 276. Calc. for $C_{14}H_{12}O_6$: C, 60·9; H, 4·4; CH_3O, 33·7% (three methoxyls); mol. wt., 276).

(*e*) *Action of Alkali on Halfordin.*—Halfordin (200 mg) was heated under reflux with 5% NaOH for 20 min and the cooled yellow solution was acidified with HCl and kept overnight in the refrigerator. The resulting precipitate of halfordic acid crystallized from water as white plates (150 mg), m.p. 152–153 °C (Found: C, 57·1; H, 4·9; CH_3O, 31·8%. Calc. for $C_{14}H_{14}O_7$: C, 57·1; H, 4·8; CH_3O, 31·6% (three methoxyls)). Halfordic acid was moderately soluble in cold ethanol and gave only an intensification of colour with ferric chloride.

(*f*) *Methylhalfordic Acid.*—Halfordin (700 mg) methylated with dimethyl sulphate according to the method of Anet, Hughes, and Ritchie (1949) gave methylhalfordic acid (550 mg), white prisms from aqueous methanol, m.p. 180–181 °C, after sintering at 175 °C (Found: C, 58·5; H, 5·4; CH_3O, 40·4%. Calc. for $C_{15}H_{16}O_7$: C, 58·4; H, 5·2; CH_3O, 40·2% (four methoxyls)).

(*g*) *Hydrogen Peroxide Oxidation of Halfordin.*—Halfordin (1 g) in 5% NaOH was oxidized with 10% H_2O_2 (30 c.c.) for 18 hr at room temperature and the reaction was completed by heating on the water-bath for 1 hr. After removal of the oxalic acid, the product, a yellow oily solid, was sublimed at 0·5 mm. Most of the oil distilled over at 120–130 °C and the white solid at 160–180 °C (block temperature). The crystalline material was resublimed at 10^{-2} mm and the sublimate crystallized from ether giving furan-2,3-dicarboxylic acid (7 mg) white needles, m.p. 217–219 °C, decomp. (lit. 220 °C, Späth and Pesta 1934; 219 °C decomp., Stoll, Pereira, and Renz 1950; 215–217 °C decomp., Caldwell and Jones 1945) (Found: C, 46·9; H, 2·7%. Calc. for $C_6H_4O_5$: C, 46·2; H, 2·6%).

(*h*) *Norhalfordin.*—Halfordin (500 mg) was heated under reflux with concentrated HCl (25 c.c.) for 20 min and the off-white crystalline solid which precipitated out was filtered off, washed, and crystallized to constant melting point from ethanol (charcoal) giving norhalfordin (236 mg), colourless highly refracting prisms, m.p. 228–228·5 °C (Found: C, 59·5; H, 4·0; CH_3O, 23·3%. Calc. for $C_{13}H_{10}O_6$: C, 59·5; H, 3·9; CH_3O, 23·6% (two methoxyls)).

Norhalfordin is very sparingly soluble in ethanol, and the solution has a yellowish green fluorescence and gives an immediate weak green ferric chloride colouration which increases in intensity to a deep olive-green after several hours. Acetylation of norhalfordin (120 mg) with acetic anhydride (5 c.c.) and acetyl chloride (0·3 c.c.) for 30 min on the water-bath gave an acetate (80 mg) which formed white plates from methanol, m.p. 173–174 °C after sintering at 165 °C (Found: C, 58·7; H, 4·0%. Calc. for $C_{15}H_{12}O_7$: C, 59·2; H, 4·0%). Ethereal diazomethane in excess was added to norhalfordin (80 mg) in methanol (10 c.c.), and 2 days later the solvent was removed under reduced pressure and the residue on crystallizing from methanol gave halfordin (65 mg), m.p. and mixed m.p. 138–139 °C.

(*i*) *Hydrogenation of Halfordin.*—Halfordin (208 mg) in glacial acetic acid (4 c.c.) was hydrogenated at atmospheric pressure at 55 °C in the presence of palladized charcoal (150 mg of 5%). Absorption of 1 mole of hydrogen was complete in 2 hr. The catalyst was filtered off, the solvent removed under reduced pressure, and the residue crystallized from methanol as white needles (180 mg), m.p. 144·5–145·5 °C (Found: C, 60·4; H, 5·1%. Calc. for $C_{14}H_{14}O_6$: C, 60·4; H, 5·0%).

An alcoholic solution of dihydrohalfordin shows a very deep blue fluorescence. Many attempts were made to prepare a tetrahydro-derivative. Adams's catalyst and Raney nickel were used under various conditions of temperature and pressure, but only a dihydro-derivative was obtained. When Raney nickel W5 was used at 5 atm pressure, the main product was an oil and a small amount (2 mg) of a substance, m.p. 182–183 °C, the phenolic properties of which indicated that it probably resulted from hydrogenolysis of the furan ring.

(*j*) *Action of Sodium Amalgam on Halfordin.*—Halfordin (400 mg) in 10% NaOH (10 c.c.) was stirred for 24 hr with Na amalgam (40 g of 5%). After removal of the Hg, the alkaline solution was acidified and gave halfordic acid (350 mg), m.p. and mixed m.p. 155–156 °C. No trace of any acidic material could be found in the filtrate.

(*k*) *Nordihydrohalfordin.*—Dihydrohalfordin (74 mg) on refluxing in concentrated HCl gave nordihydrohalfordin (40 mg) as colourless plates from methanol, m.p. 236–237 °C, an alcoholic solution of which gave the same type of ferric reaction as did norhalfordin (Found : C, 59·2 ; H, 4·5%. Calc. for $C_{13}H_{12}O_6$: C, 59·1 ; H, 4·6%).

Acetylation of nordihydrohalfordin gave an acetate, m.p. 142–142·5 °C (Found : C, 58·7 ; H, 4·6%. Calc. for $C_{15}H_{14}O_7$: C, 58·8 ; H, 4·6%). This compound was also obtained by catalytic hydrogenation of norhalfordin acetate.

(*l*) *Ozonolysis of Dihydrohalfordin.**—Dihydrohalfordin (900 mg) in glacial acetic acid (25 c.c.) and ethyl acetate (2 c.c.) was ozonized at 0 °C at the standard flow rate for 45 min. The ozonide was decomposed by pouring into boiling water and the acetic acid was neutralized with $NaHCO_3$ and the solution extracted with ether. The ether extract was worked up in the usual way to give a phenolic aldehyde which crystallized from methanol as colourless plates, m.p. 105–106 °C which were readily soluble in 1% NaOH and gave a wine-red ferric reaction in ethanolic solution (Found : C, 58·5 ; H, 5·4 ; CH_3O, 27·2%. Calc. for $C_{11}H_{12}O_5$: C, 58·9 ; H, 5·4 ; CH_3O, 27·7% (two methoxyls)).

The substance could not be methylated with ethereal diazomethane and the product from the action of methyl iodide and potassium carbonate in acetone could not be induced to crystallize.

(*m*) *Ozonolysis of Halfordin.*—(i) Halfordin (1 g) in glacial acetic acid (25 c.c.) and ethyl acetate (2 c.c.) was ozonized at 0 °C at the standard flow rate for 25 min. The ozonide was decomposed by stirring with zinc dust (0·5 g) for 10 min, and the solvent removed under reduced pressure to leave a yellow solid. This was freed of a trace of acidic material by dissolving in ether and washing with $NaHCO_3$. The product was obtained as off-white needles from ethanol (380 mg), m.p. 169–170 °C (Found : C, 55·9 ; H, 4·3 ; CH_3O, 32·4%. Calc. for $C_{13}H_{12}O_7$: C, 55·7 ; H, 4·3 ; CH_3O, 33·2% (three methoxyls)).

It formed a 2,4-dinitrophenylhydrazone, dark red needles from ethanol-ethyl acetate, m.p. 268–270 °C (decomp.) (Found : N, 12·0%. Calc. for $C_{19}H_{16}O_{10}N_4$: N, 12·2%). It gave only an intensification of colour with ferric chloride but dissolved in dilute aqueous alkali, and on treatment with methyl iodide and K_2CO_3 in acetone yielded a methyl ether which was characterized as its 2,4-dinitrophenylhydrazone—red needles, m.p. 259–260 °C (decomp.), which showed a large depression on admixture with the 2,4-dinitrophenylhydrazone of the starting material (Found : N, 11·7%. Calc. for $C_{20}H_{18}O_{10}N_4$: N, 11·8%).

(ii) Halfordin (1 g) in freshly distilled chloroform (25 c.c.) was ozonized at −5 °C for 45 min at the standard flow rate. The chloroform was removed at room temperature under reduced pressure and the pale yellow oil was dissolved in glacial acetic acid (5 c.c.) and treated with zinc dust (0·5 g) with external cooling. The acetic acid was taken off under reduced pressure and the yellow oil dissolved in ether and washed with 2% $NaHCO_3$. Removal of the ether and crystallization from aqueous methanol gave the product (IIa or IIb) (130 mg), white needles, m.p. 118–119 °C (Found : C, 53·1 ; H, 4·4%. Calc. for $C_{10}H_{10}O_6$: C, 53·1 ; H, 4·4%).

This compound gave a wine-red ferric chloride reaction, and mono-2,4-dinitrophenylhydrazone, which crystallized from methanol as deep red needles, m.p. 220–222 °C (decomp.) (Found : N, 13·8%. Calc. for $C_{16}H_{14}O_9N_4$: N, 13·8%).

(*n*) *Tetramethoxyterephthalaldehyde.*—The diphenolic dialdehyde (IIa or IIb) (115 mg) in acetone (30 c.c.) was refluxed with methyl iodide (3 c.c.) and potassium carbonate (6 g) for 18 hr. The mixture was worked up in the usual way giving tetramethoxyterephthalaldehyde (83 mg) white plates from methanol, m.p. 114–115 °C (Found : C, 57·0 ; H, 5·5 ; CH_3O, 45·0%. Calc. for $C_{12}H_{14}O_6$: C, 56·7 ; H, 5·5 ; CH_3O, 48·8%).

* All ozonolysis experiments described in the present paper were carried out at a flow rate standardized to give 11·4 mg of ozone per min.

The compound gave mono-2,4-dinitrophenylhydrazone, brilliant deep red plates from ethyl acetate, m.p. 200–201 °C (decomp.) (Found: N_2 12·8%. Calc. for $C_{18}H_{18}O_9N_4$: N, 12·9%).

(*o*) *Tetramethoxyterephthalic Acid* (*IV*; *R*=*COOH*).—Tetramethoxyterephthalaldehyde (130 mg) was suspended in water (25 c.c.) and KOH (0·2 g) added. Potassium permanganate (5% soln.) was added slowly from a burette.

After permanganate equiv. to one atom of oxygen had been taken up, the rate of oxidation slowed down and the reaction mixture was warmed to 50 °C and oxidation ceased when permanganate equiv. to two atoms of oxygen had been added. The manganese dioxide sludge was filtered off and extracted with boiling water (15 c.c.). The filtrate and washings were combined, acidified with concentrated HCl to pH 2, and extracted with ether for 18 hr. Removal of the ether gave a white crystalline solid which crystallized from ether as white plates, m.p. 276–279 °C (decomp., uncorr.) though this m.p. was somewhat dependent on the rate of heating (Found: C, 50·0; H, 5·0%. Calc. for $C_{12}H_{14}O_8$: C, 50·4; H, 4·9%).

The dimethyl ester was prepared by methylation with diazomethane and was obtained as a pale yellow oil, which was vacuum distilled before analysis (Found: C, 53·3; H, 5·3%. Calc. for $C_{14}H_{18}O_8$: C, 53·5; H, 5·8%).

(*p*) iso*Halfordin.*—*iso*Halfordin crystallizes from methanol as long shining needles arranged radially in groups of four. These crystals, on standing in methanol for several weeks, change to an apparently more stable crystalline form of orthorhombic prisms. Both forms have the same m.p. 151–152 °C. *iso*Halfordin and halfordin have similar solubilities in most solvents, and it is very difficult to separate them by fractional crystallization (Found: C, 60·8; H, 4·3; CH_3O, 32·3%; mol. wt., 276. Calc. for $C_{14}H_{12}O_6$: C, 60·9; H, 4·4; CH_3O, 33·7% (three methoxyls); mol. wt., 276).

Like halfordin, *iso*halfordin has a blue fluorescence in alcoholic solution, gives no colour with concentrated H_2SO_4, and dissolves slowly in hot dilute N OH, but, unlike halfordin, it is regenerated (m.p. and mixed m.p.) when the alkaline solution is acidified.

(*q*) *Methylisohalfordinic Acid.*—*iso*Halfordin (200 mg) methylated as in (*f*) gave methyl-*iso*halfordinic acid (146 mg), which crystallized from aqueous methanol as white plates, m.p. 138–139 °C (Found: C, 58·6; H, 5·2; CH_3O, 40·9%. Calc. for $C_{15}H_{16}O_7$: C, 58·4; H, 5·2; CH_3O, 40·2% (four methoxyls)).

The m.p. was not raised by more than 0·5 °C after six recrystallizations from boiling water, nor did heating at 150 °C for 5 min raise the m.p. (Anet, Blanks, and Hughes 1949). The m.p. of methyl*iso*halfordinic acid was depressed by 14–18 °C on admixture with methylhalfordic acid, m.p. 180–181 °C.

(*r*) *Nor*iso*halfordin.*—*iso*Halfordin (200 mg) was refluxed for 15 min with a mixture of concentrated HCl (9 c.c.) and glacial acetic acid (25 c.c.) and the product was precipitated by pouring into water (100 c.c.). Crystallization from methanol gave crude nor*iso*halfordin (122 mg) which was purified by vacuum sublimation and, finally, by crystallization from methanol as fine white needles, m.p. 200–201 °C (Found: C, 59·4; H, 4·1; CH_3O, 22·8%. Calc. for $C_{13}H_{10}O_6$: C, 59·5; H, 3·9; CH_3O, 23·6% (two methoxyls)).

Like norhalfordin, nor*iso*halfordin gave an immediate weak green ferric colouration which increased in intensity on standing, it dissolved readily in 2N Na_2CO_3 and was converted to *iso*halfordin (m.p. and mixed m.p.) with diazomethane. With acetic anhydride and acetyl chloride it formed an acetate, $C_{15}H_{12}O_7$, which crystallized from methanol in the form of white plates, m.p. 170–170·5 °C (Found: C, 58·8; H, 3·9%. Calc. for $C_{13}H_{12}O_7$: C, 59·2; H, 4·0%).

(*s*) *Dihydroisohalfordin.*—*iso*Halfordin (213 mg), hydrogenated in glacial acetic acid (5 c.c.) in the presence of Adams's catalyst (40 mg) at 55 °C, absorbed slightly less than the theoretical amount of hydrogen for one double bond. The catalyst was filtered off and the product worked up in the usual way giving dihydro*iso*halfordin (180 mg), glistening white prisms from methanol, m.p. 160–161 °C (Found: C, 60·1; H, 5·1%. Calc. for $C_{14}H_{14}O_6$: C, 60·4; H, 5·0%).

Dihydro*iso*halfordin dissolved slowly in hot aqueous alkali and was regenerated (m.p. and mixed m.p.) when the alkaline solution was acidified.

Numerous attempts to prepare a tetrahydro-derivative were unsuccessful, and attempted reduction of *iso*halfordin with Na amalgam gave only unchanged starting material (m.p. and mixed m.p.).

(*t*) *Alkaline Peroxide Oxidation of* iso*Halfordin.*—*iso*Halfordin (400 mg) was oxidized with alkaline H_2O_2 as in (*g*) and the product worked up in the same way giving furan-2,3-dicarboxylic acid (4 mg), m.p. and mixed m.p. with the product from (*g*) 217–219 °C (decomp.).

(*u*) *Ozonolysis of Dihydroisohalfordin.*—Dihydro*iso*halfordin (0·9 g) in glacial acetic acid (25 c.c.) was ozonized at the standard flow rate for 55 min and worked up in the usual way. The product was obtained as white needles (86 mg) from methanol, m.p. 88–89 °C (Found: C, 58·8; H, 5·5; CH_3O, 27·4%. Calc. for $C_{11}H_{12}O_5$: C, 58·9; H, 5·4; CH_3O, 27·7% (two methoxyls)). It was soluble in 2N NaOH and in alcoholic solution gave a green ferric colouration which became red on dilution with water.

(*v*) *Ozonolysis of* iso*Halfordin.*—(i) *iso*Halfordin (1 g) in redistilled chloroform (25 c.c.) was ozonized at 0 °C for 45 min at the standard flow rate. The ozonide was decomposed under reducing conditions and the product was obtained as white plates from methanol (308 mg), m.p. 139–140 °C (Found: C, 55·4; H, 4·3; CH_3O, 32·3%. Calc. for $C_{13}H_{12}O_7$: C, 55·7; H, 4·3; CH_3O, 33·2% (three methoxyls)). This compound dissolved in 2N NaOH and gave a wine-red colour with ferric chloride. It formed a 2,4-dinitrophenylhydrazone which crystallized from ethanol-ethyl acetate as red needles, m.p. 259–261 °C (Found: N, 12·3%. Calc. for $C_{19}H_{16}O_{10}N_4$: N, 12·2%).

(ii) *iso*Halfordin (0·9 g) in chloroform (25 c.c.) was ozonized for 75 min and the ozonide decomposed with Zn dust and acetic acid. The acetic acid was removed under reduced pressure and the orange oil was steam distilled, 300 c.c. of distillate being collected. The distillate on standing overnight in the refrigerator deposited white needles (82 mg) and a further 32 mg of the same substance was obtained by ether extraction of the distillate. Crystallization of the product from ice-cold ether gave (VIa) white needles, m.p. 114–115 °C (Found: C, 53·2; H, 4·5; OCH_3, 26·8%. Calc. for $C_{10}H_{10}O_6$: C, 53·1; H, 4·4; CH_3O, 27·5% (two methoxyls)). It gave a wine-red ferric colouration and formed mono-2,4-dinitrophenylhydrazone which crystallized from ethyl acetate as red needles, m.p. 199–201 °C (Found: N, 13·7%. Calc. for $C_{16}H_{14}O_9N_4$: N, 13·8%).

Methylation of VIa with methyl iodide and K_2CO_3 in acetone gave VII (R=CHO), white needles from ether, m.p. 109–111 °C, which gave a depression on admixture with a sample of III (R=CHO) (Found: CH_3O, 47·1%. Calc. for $C_{12}H_{14}O_6$: CH_3O, 48·8% (four methoxyls)). The brown residue in the flask after the steam distillation of VIa was acidified with dilute HCl and extracted with ether to give an aldehydo acid, $C_{10}H_{10}O_7$, which was methylated without being examined. The fully methylated product was obtained as a clear yellow oil after vacuum distillation (Found: OCH_3, 52·0%. Calc. for $C_{13}H_{16}O_7$: CH_3O, 54·5% (five methoxyls)). The 2,4-dinitrophenylhydrazone was obtained as red needles from ethyl acetate, m.p. 236–237 °C (Found: N, 11·9%. Calc. for $C_{19}H_{20}O_{10}N_4$: N, 12·1%).

(*w*) *Tetramethoxyisophthalic Acid.*—The dialdehyde (VII; R=CHO) in 2N NaOH (20 c.c.) was oxidized at 5 °C with an excess of potassium permanganate, and worked up as in (*o*). The product (VII; R=COOH) was obtained as white needles from ether, m.p. 193–194 °C, which gave no depression on admixture with a synthetic sample of tetramethoxy*iso*phthalic acid, prepared by sodium hypobromite oxidation of 5-acetyl-2,3,4,6-tetramethoxybenzoic acid (Found: C, 50·9; H, 4·7%. Calc. for $C_{12}H_{14}O_8$: C, 50·4; H, 4·9%).

The m.p. of VIII (R=COOH) was also found to be somewhat dependent on the rate of heating. A sample of VIII (R=COOH) titrated as a dicarboxylic acid, and when heated above its m.p. at water pump vacuum in the presence of Cu powder effervesced, and white needle-like crystals, m.p. 186–187 °C, sublimed up the tube. Nierenstein (1917) records the m.p. of 2,3,4,6-tetramethoxybenzoic acid as 184–186 °C; but there was insufficient material for analysis.

(*x*) *Ultraviolet Absorption Spectra.*—The ultraviolet absorption spectra were measured in redistilled ethanol at concentrations of *c* M/20,000 using a Beckmann model DU spectrophotometer.

(*y*) *Extraction of* H. kendack *Bark.*—The light petroleum extract from 2·5 kg of *H. kendack* bark gave 20 g of crystalline material, m.p. 128–132 °C. This was dissolved in benzene (600 c.c). and filtered through a short column of alumina. Removal of the benzene and crystallization of the residue from methanol (charcoal) gave halfordin (14 g), m.p. 136–137 °C undepressed on admixture with an authentic sample of the same m.p.

VI. Acknowledgments

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NEW FLAVONES FROM *PONGAMIA PINNATA* (L.) MERR.

II. THE SYNTHESIS OF COMPOUNDS "C" AND "D"

By S. K. Pavanaram* and L. Ramachandra Row*

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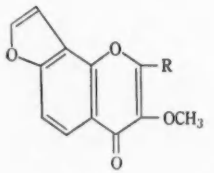
Summary

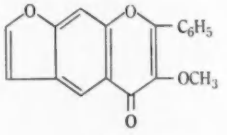
The furanoflavones, "C" and "D" of *Pongamia pinnata* (L.) Merr., now named gamatin and pinnatin, were identified by synthesis as 5-methoxy-3″,4″-methylenedioxyfurano-(3′,2′,6,7)-flavone and 5-methoxyfurano-(3′,2′,6,7)-flavone respectively. In the course of the work 5-methoxy-3″,4″-methylenedioxyfurano-(2′,3′,7,8)-flavone and 5-methoxyfurano-(2′,3′,7,8)-flavone were also synthesized.

I. Introduction

In the first paper of this series (Ramachandra Row 1952†), the isolation of two furanoflavones, karanjin (I ; R=C_6H_5) and its methylenedioxy-derivative pongapin (I ; R=3,4-(CH_2O_2)=C_6H_3) from the roots of *Pongamia pinnata* (L.) Merr. was reported. Two new furanoflavones, "C" and "D", now named gamatin and pinnatin, which were respectively isomeric with pongapin and karanjin, were also obtained. Pavanaram and Row (1955) synthesized II, the linear isomer of karanjin, but found that it was not identical with pinnatin. As it then seemed likely that pinnatin and gamatin were unsubstituted at the 3-position, syntheses of the phloroglucinol derivatives III and IV were undertaken. For these syntheses the method of Baker-Venkataraman (Baker 1933 ;



(I)



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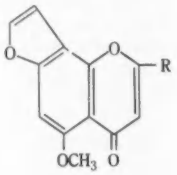

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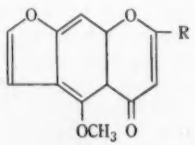

(IV)

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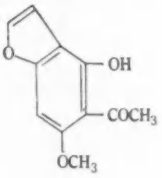
† This is regarded as Part I of this series.

Mahal and Venkataraman 1934; Baker and Simmonds 1940) was chosen in preference to that of Allan and Robinson as the latter is known to give rise to undesirable 3-acylflavones which are difficult to hydrolyse (Baker 1933; Sugasawa 1934).

5-Acetyl-4-hydroxy-6-methoxycoumarone (V) (Phillips, Robertson, and Whalley 1952) was converted to its *O*-benzoyl derivative (VI; R=C_6H_5) which was smoothly rearranged to the diketone (VII; R=6_6H_5) on shaking with solid potassium hydroxide and pyridine (Gallagher *et al.* 1953). Treatment of the diketone with glacial acetic acid containing a few drops of concentrated



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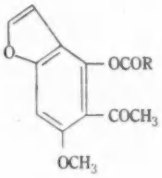
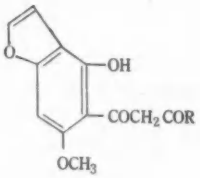


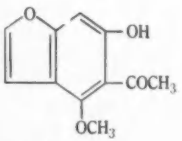
(VI)



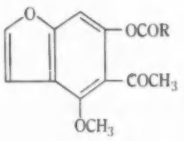
(VII)

hydrochloric acid then furnished (III; R=C_6H_5). It had m.p. 180–181 °C depressed to 130–145 °C by admixture with pinnatin of m.p. 177–179 °C. In a similar manner the *O*-piperonoyl derivative of V was converted to III (R=3,4-(CH_2O_2)=C_6H_3), m.p. 263–264 °C, obviously different from gamatin, m.p. 232–234 °C.

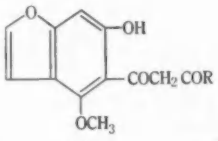
The starting material for the preparation of the linear isomers was visnagin which was converted by alkaline degradation to visnaginone (VIII) (Späth and Gruber 1941). The *O*-benzoyl derivative (IX; R=C_6H_5) of the latter was



(VIII)



(IX)



(X)

converted to the diketone (X; R=C_6H_5) which was cyclized to (IV; R=C_6H_5). The product had m.p. 180–181 °C alone or mixed with natural pinnatin but unlike the natural flavone it gave a yellow colour with concentrated sulphuric acid which became very light green on warming.* By a similar series of reactions gamatin was synthesized from the *O*-piperonoyl derivative of visnaginone.

The ultraviolet absorption spectra of natural and synthetic samples of pinnatin and of gamatin were measured in 95 per cent. ethanol using a Hilger Uvispek photoelectric spectrophotometer. The results given in Table 1 and

* After this synthesis had been completed it was found that Professor A. Schönberg of Cairo University had also synthesized pinnatin from visnaginone.

Figure 1 provide further evidence for the identity of the natural and synthetic materials. The wavelengths and the intensities correspond to a remarkable degree with those of the isomeric karanjin and pongapin respectively (Ramachandra Row 1952). It appears therefore that the position of the furan ring

TABLE 1

ULTRAVIOLET ABSORPTION DATA

Compound	$\lambda_{max.}$ (mμ)	Log $\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	Log $\varepsilon_{max.}$
Pinnatin	269	4·52	305	4·19
Gamatin	251·5	4·52	334	4·39

in the molecule does not affect the spectrum to any marked degree. The spectrum of visnagin (Bailey, Geary, and de Wald 1951) shows three main bands at 243, 275, and 322·5 mμ. The replacement of the 2-methyl group by a phenyl residue as in pinnatin appears to bring about a merger of the first two bands.

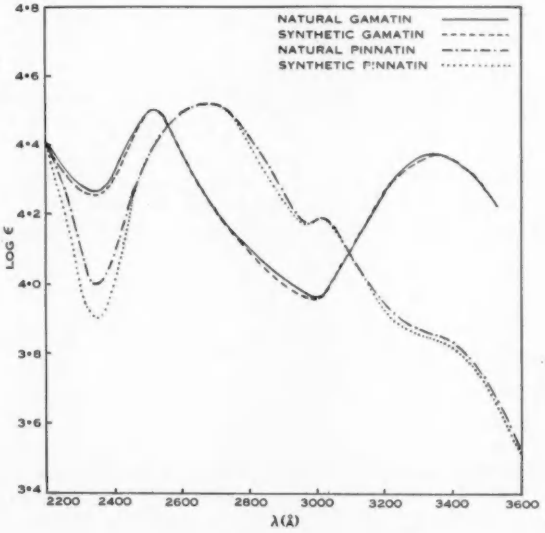


Fig. 1

With the establishment of the structures of pinnatin and gamatin as linear, a new class of furanoflavones has come to light as hitherto only the angular furanoflavones, karanjin, pongapin, and lanceolatin B, isolated from the roots of *Tephrosia lanceolata* Grab. (Rangaswami and Sastry 1955), were known to occur naturally. The latter are derived from resorcinol whilst the former are based on phloroglucinol.

II. Experimental

Melting points are uncorrected.

(*a*) *5-Methoxyfurano-(2′,3′,7,8)-flavone.*—(i) 5-Acetyl-4-hydroxy-6-methoxycoumarone (0·8 g) was benzoylated with benzoyl chloride (0·6 ml) and dry pyridine (3·5 ml) with cooling to 0 °C. After keeping for 2 hr at room temperature (30 °C) the mixture was poured into ice-cold hydrochloric acid. The product (yield 82%) purified by crystallization from benzene and then light petroleum (b.p. 40–60 °C) was obtained as thin colourless rectangular laminae, m.p. 120–121 °C, which gave a negative ferric reaction (Found : C, 69·6 ; H, 4·3%. Calc. for $C_{18}H_{14}O_5$: C, 69·7 ; H, 4·6%).

(ii) The benzoate (1 g) was shaken for 1 hr with dry pyridine (4 ml) and powdered potassium hydroxide (0·8 g) at 40 °C. The bright yellow solid mixture was treated with excess 20% acetic acid and kept overnight. The yellow diketone was collected and crystallized twice from benzene-light petroleum to give bright yellow prisms (yield 0·55 g), m.p. 130–131 °C, which gave a brownish green ferric reaction (Found : C, 69·7 ; H, 4·5%).

(iii) The diketone (0·45 g) was refluxed with glacial acetic acid (15 ml) containing a few drops of concentrated hydrochloric acid for 3 min. The colour of the solution changed to deep red and finally became pale. By the careful addition of water, the product was precipitated as a colourless solid. Crystallization from benzene-light petroleum (twice) and then from light petroleum (b.p. 40–60 °C) gave fine needles (0·2 g), m.p. 180–181 °C depressed to 130–145 °C on admixture with natural pinnatin (Found : C, 73·7 ; H, 4·1%. Calc. for $C_{18}H_{12}O_4$: C, 74·0 ; H, 4·1%). The ferric reaction was negative. On treating with concentrated sulphuric acid and warming the colour changed from yellow to green, then to blue, and finally, to brown.

(*b*) *5-Methoxy-3″,4″-methylenedioxyfurano-(2′,3′,7,8)-flavone.*—(i) Acylation of V with piperonoyl chloride was effected as above. The product, which gave a negative ferric reaction, was crystallized from acetone-light petroleum and then light petroleum and obtained as fine colourless needles, m.p. 117–118 °C (Found : C, 64·4 ; H, 4·1%. Calc. for $C_{19}H_{14}O_7$: C, 64·4 ; H, 4·0%).

(ii) The piperonoyl derivative was rearranged to the diketone at 40 °C during 3 hr as above. The crude product recrystallized from acetone-light petroleum and then from methanol gave stout yellow prisms, m.p. 151–152 °C, which had a greenish brown ferric reaction (Found : C, 64·4 ; H, 4·1%).

(iii) The diketone was cyclized to the flavone as above. Two crystallizations from ethanol and one from glacial acetic acid gave the pure product as bundles of thin colourless needles, m.p. 263–264 °C (Found : C, 67·8 ; H, 3·7%. Calc. for $C_{19}H_{12}O_6$: C, 67·9 ; H, 3·6%). The ferric reaction was negative. The sulphuric acid reaction was initially yellow changing rapidly to green then blue and finally to brown on warming. Gallic acid and concentrated sulphuric acid gave a greenish blue colour.

(*c*) *Pinnatin.*—(i) Benzoylation of visnaginone was effected as usual. The product which had a negative ferric reaction crystallized from methanol in thin transparent rectangular plates, m.p. 105–106 °C (Found : C, 69·2 ; H, 4·8%. Calc. for $C_{18}H_{14}O_5$: C, 69·7 ; H, 4·6%).

(ii) Rearrangement to the diketone was carried out at 40 °C for 4 hr in the usual manner. The product crystallized from benzene-light petroleum as stout rectangular prisms, m.p. 109–111 °C, which gave a brown ferric test (Found : C, 69·7 ; H, 4·7%).

(iii) Cyclization of the diketone to the flavone was accomplished in the usual way. The product was still pale yellow after two crystallizations from methanol and was further purified by passing a benzene solution through a column of alumina. The material eluted by benzene-ethanol (1 : 1) on crystallization from ethanol then gave colourless rectangular prisms showing a tendency to taper at one end, m.p. 181–182 °C undepressed by admixture with natural pinnatin of m.p. 177–179 °C (Found : C, 73·8 ; H, 4·1%. Calc. for $C_{18}H_{12}O_4$: C, 74·0 ; H, 4·1%). The ferric reaction was negative and the yellow colour formed with concentrated sulphuric acid became only faintly green on warming.

(*d*) *Gamatin.*—(i) A mixture of visnaginone (0·2 g) and piperonoyl chloride (0·26 g) was treated with pyridine (3 ml) and heated to 50 °C for 10 min. After keeping overnight, the product

was worked up in the usual way. The substance (0·12 g) which gave a negative ferric test crystallized from ethanol as thin transparent rectangular plates, m.p. 150–151 °C (Found: C, 64·6; H, 4·3%. Calc. for $C_{19}H_{14}O_7$: C, 64·4; H, 4·0%).

(ii) Rearrangement to the diketone was effected as usual. The crude sticky product after two crystallizations from methanol gave stout yellow prisms, m.p. 121–123 °C (Found: C, 64·3; H, 4·3%). The ferric reaction was brown.

(iii) Cyclization to the flavone and purification of the product was effected as in Section II (c) (iii). The substance crystallized from ethanol as very pale yellow silky needles, m.p. 233–234 °C alone or mixed with natural gamatin (Found: C, 67·4; H, 3·8%. Calc. for $C_{19}H_{12}O_6$: C, 67·9; H, 3·6%). The ferric reaction was negative. With concentrated sulphuric acid a light yellowish green colour was produced, and with sulphuric and gallic acids a greenish blue colour.

III. Acknowledgments

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SHORT COMMUNICATIONS

THE INFRA-RED SPECTRA OF SOME MIXED BORATE ESTERS*

By R. L. WERNER† and K. G. O'BRIEN‡

In a recent paper|| the infra-red spectra of a series of borate esters have been reported and a strong band at 1340 ± 10 cm^{-1} has been assigned to the B—O stretching frequency.

In connection with work on Boroxole compounds, which will be presented separately, it has been found possible to prepare a series of mixed borate esters of the general formula $(R_1O)(R_2O)_2B$ and the infra-red spectra of these compounds have been examined. In Table 1 the frequencies of the absorption peaks (in wave numbers) of these compounds are given and in Figure 1 the

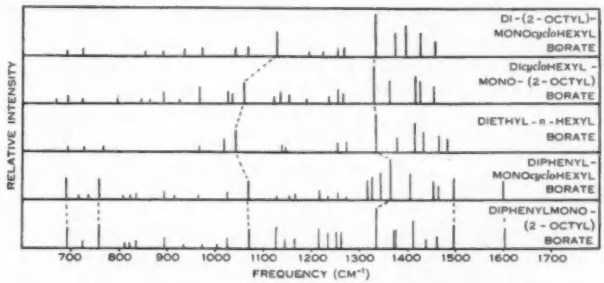

Fig. 1.—The relation of corresponding bands in the infra-red spectra of some asymmetrical borate esters.

relationship of bands is shown. Comparison of these spectra with those obtained earlier shows a similar strong band due to the B—O link, within the range previously reported, except in the case of diphenylmono*cyclo*hexyl borate which is somewhat higher at 1363 cm^{-1}. A tendency of the aryl esters to give rise to a somewhat high value is apparent also in the earlier data|| although the diphenyl mono-(2-octyl)borate now reported is anomalous in this respect.

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|| Werner, R. L., and O'Brien, K. G. (1955).—*Aust. J. Chem.* **8**: 355.

It is a reasonable inference from the results obtained in the two series of compounds studied, that the B—O band would give rise to a similar band in esters

TABLE 1

THE INFRA-RED SPECTRA OF SOME BORATE ESTERS

Samples were run as capillary film

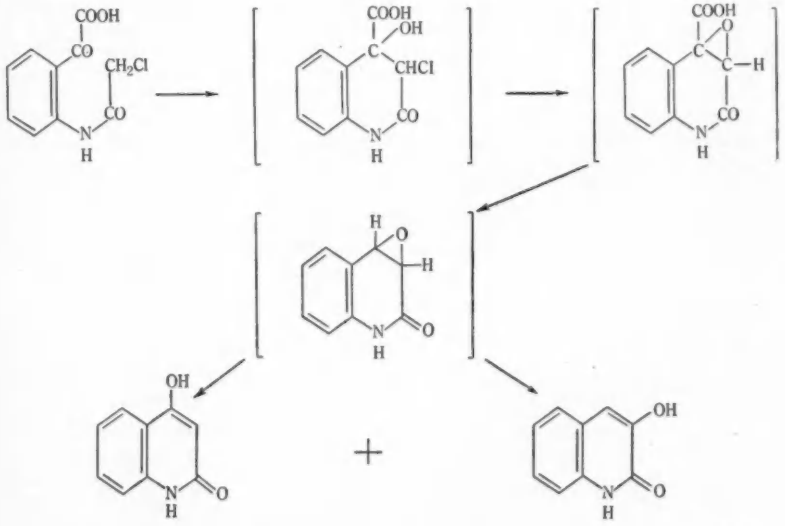
Di-(2-octyl)-mono-*cyclo*hexyl Borate	Di*cyclo*hexyl-mono-(2-octyl) Borate	Diethyl *n*-Hexyl Borate	Diphenyl-mono-*cyclo*hexyl Borate	Diphenyl-mono-(2-octyl) Borate	Assignment
			1600 (s)	1601 (s)	Phenyl
			1496 (s)	1498 (s)	Phenyl
		1482 (m)	1466 (w)	1460 (m)	
1458 (m)	1452 (m)	1466 (m)	1451 (m)	1440 (m)	C—H bending
1426 (m)	1428 (ms)	1431 (ms)			
1397 (s)	1416 (s)	1414 (s)	1405 (s)	1411 (s)	
1376 (m)	1361 (ms)	1379 (w)		1376, 1371 (ms)	
1332 (vs)	1330 (vs)	1333 (vs)	1363 (vs)	1336 (vs)	B—O stretching
1268 (w)	1266 (w)		1343 (s)	1262, 1252 (m)	
1254 (w)	1255 (m)		1327, 1318 (ms)	1235 (m)	
1225 (w)	1236 (w)	1271 (w)	1272, 1256 (w)	1216 (ms)	
		1252 (w)	1236 (w)		
1194 (w)	1190 (w)		1216 (m)		
	1152 (mw)	1146 (w)	1165, 1152 (w)	1165, 1145 (w)	
	1133 (m) 1120 (mw)	1138 (w)	1129 (w)	1127 (m)	
1129 (ms) 1068 (mw)	1060 (ms)	1040 (ms)	1069 (ms)	1070 (ms)	C—O stretching
1040 (w)	1035 (w)		1035 (w)		
	1025 (mw)	1019 (w)	1023 (mw)	1023 (m) 1003 (w)	
971 (w)	968 (m)	967 (w)	965 (w)	973 (w)	
933 (w)	925 (w)		925, 915 (w)	931 (w)	
890 (w)	891 (m)		895 (mw)	896 (mw)	
851 (w)	852, 845 (w)		836, 821, 810 (w)	835, 821, 811 (w)	
	797, 785 (w)		759 (s)	759 (s)	Phenyl
723 (w)	724 (w)	769, 728 (w)	736, 718 (w)	723 (m)	
690 (w)	692 (w) 670 (w)	691 (w)	691 (s)	691 (s)	Phenyl

of the type $R_1R_2R_3O_3B$ and in other compounds in which the BO_3 group is presumed to exist, such as the trialkoxyboroxoles.

THE REACTION OF *N*-CHLOROACETYLISATIN WITH ALKALI*

By J. R. Price† and L. W. Smith†

A simple laboratory synthesis of 4-hydroxy-2-quinolone based on the Camps method for preparing 2-quinolone-4-carboxylic acids from acylisatins has been described by Huntress and Bornstein (1949), who claim that reaction of *N*-chloroacetylisatin with alkali gives 56–70 per cent. yields of crude 4-hydroxy-2-quinolone. In our hands this reaction always leads to a mixture of 4-hydroxy-2-quinolone, in about 15 per cent. yield, with an approximately equal amount of an isomeric substance, m.p. 265 °C. The low yields of purified products are due to hydrolysis of the chloroacetyl compound, 55–65 per cent. being recoverable as isatin.



The second product is 3-hydroxy-2-quinolone (2,3-dihydroxyquinoline), the identity of which was established by comparison with a specimen prepared by the action of diazomethane on isatin (Arndt, Eistert, and Ender 1929). Formation of both 3- and 4-hydroxyquinolones in this reaction is of interest, particularly as *N*-acetylisatins (see, e.g. Halberkann 1921) give rise to 2-quinolone-4-carboxylic acids. A satisfactory explanation of the course of

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the reaction must therefore account for both the decarboxylation and the formation of an intermediate which can be converted to either 3- or 4-hydroxy-2-quinolone. These requirements are met by the following scheme* involving ethylene oxide formation and consequent ready decarboxylation of the intermediate glycidic acid (see, e.g. Barbier 1934).

Experimental

Microanalyses were carried out in the C.S.I.R.O. Microanalytical Laboratory. All melting points are corrected.

Reaction of *N*-chloroacetylisatin with alkali was carried out as described by Huntress and Bornstein (loc. cit.), but acidification was effected in two stages. 10N hydrochloric acid (6 ml) added to the reaction mixture from *N*-chloroacetylisatin (5 g), sodium hydroxide (5 g), and water (150 ml) gave a white precipitate (1·3 g, m.p. 250–320 °C) consisting mainly of 3- and 4-hydroxy-2-quinolones. A precipitate (2·2 g), which was essentially isatin, formed on further acidification.

Crude 4-hydroxy-2-quinolone was separated from the first precipitate by crystallization from methanol in which it is only sparingly soluble. Recrystallization from a large volume of methanol gave 4-hydroxy-2-quinolone as colourless needles, m.p. 361–362 °C (decomp.) (Found : C, 67·3 ; H, 4·4 ; N, 8·7%. Calc. for $C_9H_7O_2N$: C, 67·1 ; H, 4·4 ; N, 8·7%). The nitroso-derivative melted at 217 °C (decomp.), the acetyl-derivative at 221–222 °C. 4-Hydroxy-2-quinolone, prepared by the method of Ashley, Perkin, and Robinson (1930) from methyl acetylanthranilate, melted at 360–361 °C (decomp.), its nitroso derivative at 216 °C (decomp.), and its acetyl derivative at 221–222 °C. These melting points were unchanged in admixture with the corresponding materials prepared from *N*-chloroacetylisatin. 4-Hydroxy-2-quinolone gives a weak orange Fe^{3+} reaction.

Crude 3-hydroxy-2-quinolone from the methanolic liquors could not be further purified by crystallization. Acetylation with acetic anhydride and pyridine gave the acetyl-derivative, colourless needles from ethanol, m.p. 216·5–217·5 °C alone or mixed with authentic 3-acetoxy-2-quinolone, m.p. 217·5–218·5 °C (Found : C, 65·3 ; H, 4·5%. Calc. for $C_{11}H_9O_3N$: C, 65·0 ; H, 4·4%). Alkaline hydrolysis of the acetyl-derivative gave 3-hydroxy-2-quinolone, colourless needles from methanol, m.p. 264–265 °C, mixed m.p. with a specimen prepared according to Arndt, Eistert, and Ender (loc. cit.) 265–266 °C (Found : C, 67·1 ; H, 4·4 ; N, 9·0%. Calc. for $C_9H_7O_2N$: C, 67·1 ; H, 4·4 ; N, 8·7%). The substance gives a blue-green Fe^{3+} reaction.

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* Developed in the course of discussion with Professor D. S. Tarbell, Department of Chemistry, University of Rochester, Rochester 3, N.Y.

Corrigenda

Volume 7, Number 3, Pages 264–8

Liquid-Vapour Equilibria. IV. The System Ethanol+Benzene at 45 °C. By I. Brown and F. Smith

Volume 8, Number 4, Pages 501–5

Liquid-Vapour Equilibria. VII. The Systems Nitromethane+Benzene and Nitromethane+Carbon Tetrachloride at 45 °C. By I. Brown and F. Smith

Volume 8, Number 3, Pages 361–9

Heats of Mixing of Alcohol Solutions. By I. Brown and W. Fock

The density values of some pure components, with densities below 1·0, given in the above three papers are low. In Table 1 of the first two papers the density (d_4^{25}) of benzene was given as 0·87359 and 0·087366 respectively; these should be 0·87366. In Table 1 of the third paper the following corrections apply:

Benzene: *For* 0·87359 *read* 0·87364.
Acetone: *For* 0·78494 *read* 0·78501.
2,2,4-Trimethylpentane: *For* 0·68766 *read* 0·68778.

These errors were brought about by the use of a table of buoyancy corrections given by Roeder (1953). His method greatly simplified the calculation of the corrections. Unfortunately, the values of the corrections given in Table 1 of his paper apply only to densities from 1·00 to 1·50 and not also to densities below 1·0 as he states.

The values given in his table were calculated from his expression $d=P'/V+K$, where d is the corrected density, P' is the difference in weights of the full and empty pyknometer, and V is the true volume of the pyknometer in ml. The correction factor K is given by

$$K=\lambda\left(1-\frac{P'}{V}\cdot\frac{1}{\sigma}\right),$$

where λ is the air density, assumed to be the same at the two weighings, and σ is the density of the weights (8·4 for the tabulated values given).

Densities calculated by these formulae are correct to 3 in the fifth decimal place provided the air density at the two weighings does not differ by more than 0·000005.

A correct set of K values for densities less than 1·00 can be calculated from the formula. As an example, for an air density of 0·00120 the correction for a P'/V of 1·50 would be 0·00099, while that for a P'/V of 0·50 would be 0·00113 and not 0·00099 as given in Roeder's table.

To confirm the density of highly purified benzene two separate samples were prepared by the method of Brown and Ewald (1951) with an additional fractional distillation before crystallization. The freezing curve of these samples was measured in an apparatus the same as that of Herington and Handley (1950) using a calibrated platinum resistance thermometer and a calibrated Mueller bridge. The purity of the benzene was determined by the method of Mair, Glasgow, and Rossini (1941). The densities were measured by the method of Brown and Ewald (1950) and the refractive indices using a calibrated Hilger-Chance precision refractometer.

Benzene Sample	Purity Mol. (%)	$d_4^{25\cdot00}$	$n_D^{25\cdot00}$
A	99·98 ± 0·01	0·87374	1·49799
B	99·98	0·87370	1·49801

The accuracy of the thermodynamic data reported in the above papers is unaffected by these density errors as density values were not used for analysis but only as criteria of purity of the components.

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